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HYPERTENSION IN CHILDREN*

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HYPERTENSION in children, although uncommon, may present vexing problems of diagnosis and management. During the past several years a number of children have been referred to The Hospital for Sick Children suffering from disease in which hypertension has been a prominent finding. In the light of these experiences, some salient features generally applicable to children are considered, with special reference to differential examination and diagnosis, special investigation and therapy. Eight clinical examples which emphasize therapeutic problems are reviewed.

HYPERTENSION IN CHILDREN VERSUS ADULTS

Most causes of elevated blood pressure are common to both children and adults, e.g. diseases of the renal, endocrine and central nervous systems. Certain notable exceptions differentiate the two age groups. Essential hypertension, the commonest cause of persistently elevated blood pressure in adults, is rarely found in childhood. In contrast, coarctation of the aorta and Wilms' tumour are problems of the young. Furthermore, emphasis should be placed upon the importance of recognizing adolescent hypertension, uncommon though it be, since 60% of the patients falling into this group have been tentatively defined as labile hypertensives or hypertensive reactors, there being no evidence of organic disease.[1] In such a child, a family history of hypertension constitutes an indication for careful periodic observations through the stage of growth and development.

INTERPRETATION OF HIGH PRESSURE READINGS

Three factors influence the interpretation of blood pressure readings in children:

(a) The blood pressure rises progressively during growth and development from neonatal levels of approximately 80/46 mm. Hg to adult levels about the time of puberty. The average value for each age group is listed in the footnote of Table III.

(b) The cuff should cover about two-thirds of the upper arm. The blood pressure reading is dependent in part on the cuff width, since undersized cuffs result in falsely high values and vice versa.

(c) Apprehension, excitement and previous exercise may cause elevation of the blood pressure. A bottle for the baby to suck or a lollipop for an apprehensive child, as well as repeated pressure readings, assists in defining the true values.

Of special note is the importance of defining localized blood pressure elevations, as in coarctation of the aorta. Palpation of the femoral arteries is a prime requisite.

DIFFERENTIAL DIAGNOSIS

A determination of the blood pressure is frequently omitted from the physical examination of children in view of the considerations outlined above, and because of the common impression that hypertension is not an important problem in children. The etiology of hypertension may be immediately apparent, as in a child suffering from acute glomerulonephritis, but there are occasions when unrecognized disease may become apparent only as a result of the complications of hypertension. Such an enigma was presented recently when a 12-year-old boy, believed well, developed a sudden left hemiplegia associated with an intracerebral hæmorrhage. The blood pressure was found elevated to 190/160 mm. Hg and did not fall in the weeks following evacuation of the occipital clot. Complete investigations have failed to clarify which situation was antecedent, the hypertension or the hæmorrhage.

Since a routine physical examination usually progresses from head to toe, we have adopted a geographical approach to the differential diagnosis of hypertension. Such a method is illustrated in Fig. 1, which depicts the key anatomical structures considered sequentially during examination, and certain associated disorders causing hypertension. In most instances the cause is readily apparent after the history and physical examination are recorded.

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Factors in the Differential Diagnosis and Management of Hypertension

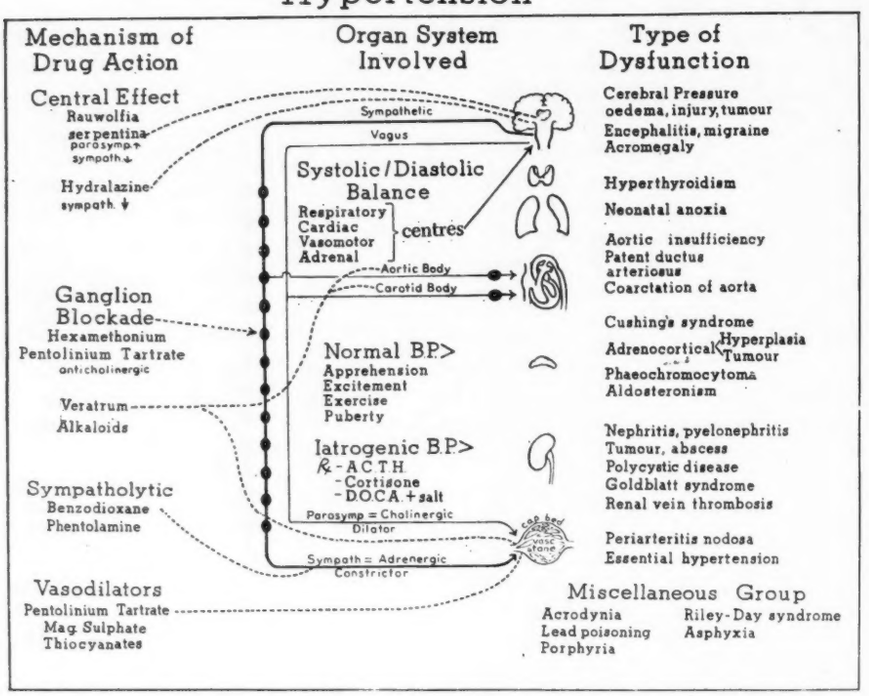

Fig. 1.—The schema presents a working classification for investigation and treatment of hypertension.

Special attention to the adequacy of renal function is necessary, since renal dysfunction is the commonest cause of hypertension in childhood. In fact, the greatest difficulty in differential diagnosis arises from the interpretation of renal function tests, since hypertension alone, in due course, will cause renal dysfunction. It is from this area that much misunderstanding has stemmed in the past and for which improved diagnostic procedures now available have been of great assistance. For instance, the diagnosis of essential hypertension can be made only after the definite exclusion of all other diseases which may be associated with hypertension. These have been considered in reviews by Haggerty *et al.*[2] and McCrory.[3] As depicted in Fig. 1, these include diseases of the central nervous system, abnormalities of cardiac development, certain hormonal dysfunctions of adrenal and sympathetic origin, and heavy metal poisoning.

INVESTIGATIONS

Certain observations made initially by the physician may establish the etiology of the hypertension. These are noted in Table I, in addition to further tests which may have to be done later in order to clarify the situation.

Most of these techniques can be carried out directly under the supervision of the family doctor. However, certain of the procedures can be accurately conducted and assessed only in special hospital units. Cardiac catheterization and aortography require special facilities. Likewise, in order to make valid measurements of aldosterone excretion, the sodium intake must be carefully controlled.

Unilateral (split) renal function tests may provide assistance in defining a unilateral pyelonephritis or vascular anomaly which may be causing

TABLE I.

Body functions to be investigated	*Initial studies*	*Later studies*
Renal	—Repeated urinalyses—microscopic search of centrifuged specimens for casts and cells. —Urine culture (catheter). —Concentration test (if B.U.N. not above 40 mg.%). —Intravenous pyelogram (following conc. test and if B.U.N. not above 40 mg.%). —Creatinine and urea clearance.	—Retrograde urography including individual ureteral tests for: (1) culture (2) volume (3) sodium concentration —Aortography —Percutaneous biopsy
Cardiovascular	—Radiograph of heart, 6 foot plate (P.A. and lateral). —Electrocardiogram. —Femoral pulsation, B.P. arms vs. legs. —Status of vessels—funduscopic examination.	—Barium œsophagogram. —Cardiac catheterization. —Aortography.
Adrenal	—17-Ketosteroid excretion.	—Aldosterone excretion.
Sympathetic ganglionic centres	—Phentolamine (Regitine) test.	—Urinary catecholamine excretion.
Neurological	—Lumbar puncture (if encephalitis or poliomyelitis suspected). —Skull x-rays (tumour).	—Electroencephalogram. —Pneumoencephalogram. —Ventriculogram.
Poisoning	—Lead—blood smear—stippled cells —anæmia, glycosuria —x-ray long bones for lead lines.	—Lead—24-hour urine excretion including coproporphyrin —Mercury—24-hour urine excretion.

secondary hypertension. The test relies upon differences in output of sodium and of water by each kidney when the patient has had a moderate sodium load* for two days before examination, and an intravenous infusion of 5% glucose in water before and during the collection of specimens from the ureters. Under normal circumstances there should be less than 10% difference in the sodium and water excretions from each side. Renal arterial disease may be associated with at least a 50% decrease in water and a 15% decrease in sodium from the affected side. Similarly, unilateral pyelonephritis may result in diminished volume and sodium excretion from the affected side. Limited experience has indicated that nephrectomy under these circumstances may be of benefit; in contrast, pyelonephritis associated with decreased volume and increased sodium concentration from the affected side is unlikely to benefit. Recent experiences with this procedure in adults are being reported by Yendt *et al.*[4]

Howard *et al.*[5] have reviewed this subject and indicated the caution with which one must interpret "split" renal function studies because of the possibility of leakage around the ureteral catheter or of alteration in renal function induced by the ureteral catheterization. The limited experience with this procedure in children makes the question of interpretations difficult; if doubt exists, aortography must still be performed for visualization of the renal arterial flow.

The role of the salt-retaining adrenocortical hormone, aldosterone, in the production of hypertension is not clear; it may be excreted in increased amounts in a variety of conditions associated with fluid retention. The occurrence of a primary aldosterone-secreting tumour of the adrenal gland, as described by Conn and Louis[6] in adults, has not yet been described in children. Aldosteroma causes hypertension and sodium retention without œdema. However, a few children have been observed with bilateral adrenal hyperplasia in which the findings mimicked those of aldosteroma.[7, 8] Partial adrenalectomy has been the therapy of choice in these instances. Since elevated aldosterone excretion may be found in adults with essential hypertension, Genest[9] has advanced the suggestion that this state may be an expression of chronic mild hyperaldosteronism. Interpretation of increased aldosterone secretion remains difficult, and because of the laborious methods of measurement must be restricted to carefully chosen cases.

General Principles of Therapy

Management of hypertension is based upon two tenets: (1) correction of the underlying cause, and (2) treatment of the hypertension *per se*.

*Suggested salt load is sodium chloride 0.5 g. per 10 lb. of body weight for two days in addition to the salt in a normal diet.

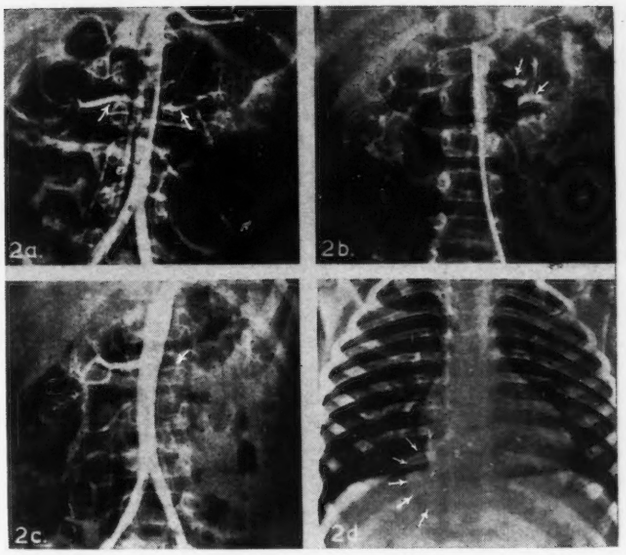

Fig. 2.—Visual definition of renal vasculature by means of aortography is usually the last investigation to be made. 2a illustrates a normal renal arterial tree; 2b shows a constrictive anomaly of the left renal artery with two dilated vascular sacs (Case 4); 2c reveals absence of blood flow through the left renal artery (Case 3); in 2d, the appearance of the mass gave the clue to localization of the phæochromocytoma in Case 5.

It is apparent from the foregoing considerations of differential diagnosis that hypertension in children is usually a secondary phenomenon. Thus treatment of the hypertension is only one phase of the management of the entire disease state, as in acute or chronic nephritis. In contrast, correction of a distorted renal artery (Fig. 2b) or removal of a phæochromocytoma (Fig. 2d) requires surgical intervention.

In the direct management of hypertension, it is advisable to limit any physical activity which causes headache, dyspnœa, chest pain or palpitation. Rigid salt restriction as a long-range therapy has usually been impracticable in young children.

Hypotensive drug therapy is the only reliable form of therapy. The preparations most commonly employed at this hospital are listed in Table II. Wilkins[10] has emphasized the importance of using the safest and mildest drugs producing the least symptoms. This is best done with small doses of drugs in combination, ascertained by repeated observation and titration on each patient.

Periodic reassessment of the influence of chronic hypertension upon vascular and renal functions should be made every six to twelve months by observing (1) the vessels of the eyegrounds by ophthalmoscopy, (2) cardiac function by E.C.G., etc., and (3) renal function by urinalysis and determination of creatinine and urea clearances.

Hypertension Complicating Acute Nephritis

While some degree of hypertension occurs in nearly every patient with acute hæmorrhagic glomerulonephritis, certain of these patients may develop grave hypertensive crises. Manifested by headache, nausea, and some clouding of vision and

TABLE II.

Drug	Site of action	Drug		Symptoms and Signs of toxicity
		Initial	Maintenance	
Reserpine (Serpasil)	Central	0.1-0.25 t.i.d.	Up to 1.0 mg./day	Laxative, nasal congestion, sedation, bradycardia
Hydralazine (Apresoline)	Central peripheral vasodilation	P.O. 10-20 mg. q.i.d. (i.m. 0.2 mg./kg. q.i.d.)	Incr. to tolerance 100 mg. q.i.d.	Lupus, arthritic syndr., headache, dizziness, hypotension, nausea, vomiting
Pentolinium tartrate (Ansolysen)	Ganglion blockade	P.O. 10 mg./day	Incr. to tolerance by single daily dosage	Postural hypotension, urinary retention, constipation, dry mouth
Chlorothiazide (Diuril)	Sodium excretion Other?	125 mg. b.i.d.-t.i.d.	Incr. to 2 g./day	Potassium depletion (especially if patient receiving low sodium intake)
Magnesium sulfate	Vasodilation		50% i.m. 1 c.c./10 lb. q.6.h. 1% i.v. 100-200 drops/min.	Hypotension and respiratory depression Antidote: calcium gluconate

consciousness, this complication is a medical emergency which requires immediate therapy. One of the chief problems of management of acute nephritis is the inability to predict, from one patient to the next, which individual may develop this complication. There is very little, if any, correlation between the degree of elevation of blood pressure (systolic and diastolic) and the onset of hypertensive encephalopathy. The rapidity of onset of hypertensive crisis (within two or three hours) during the early phase of acute nephritis provides a further unpredictable hazard. Magnesium sulfate intramuscularly, or intravenously if desired, has been the most commonly used hypotensive agent because of its rapid effect. However, treatment by this method requires careful supervision, since conscientious but overzealous therapy during a crisis may cause toxic cardiac and respiratory depression (Table II).

Etteldorf[11] has suggested an alternative therapy for nephritic hypertension which provides a wider margin of safety than magnesium sulfate. Oral or parenteral administration of reserpine, 0.01 mg./lb., and hydralazine (Apresoline), 0.3 mg./lb., per day, in divided doses, will provide a hypotensive effect. The particular value of this form of hypotensive medication is that it provides a wide range of safety, produces little or no decrease in renal function, and can be readily administered at the earliest sign of trouble, or as prophylaxis if close supervision by the physician is not possible.

CASE REPORTS ILLUSTRATING CLINICAL PROBLEMS OF HYPERTENSION

The following brief case reports illustrate a variety of ways in which hypertension can become apparent as a complication of different diseases. More complete information on each patient appears in Table III.

The first two cases reveal the problem of long-standing unrecognized pyelonephritis presenting symptoms only in advanced stages of the disease.

CASE 1.—L.S., female, 13 years, complained of intermittent headaches for three years; these had become more frequent and severe for six months before admission. There was no past history of renal dysfunction, although the mother suffered from hypertensive renal disease. Examination was not contributory except for blood pressures ranging as high as 220/172 mm. Hg and ophthalmoscopic examination which revealed a grade 2 retinopathy. Repeated urinalyses were negative. Thus, routine examination in the family physician's office was not immediately suggestive of renal disease. Subsequent investigation in hospital revealed a barely perceptible trace of proteinuria, blood urea nitrogen elevated to 84 mg. %, and markedly impaired renal function. Percutaneous renal biopsy subsequently revealed advanced interstitial fibrosis. Although urine cultures were negative, clinical and pathological features suggested chronic pyelonephritis. It is also possible that the condition is a type of familial renal disease. A moderate hypotensive response to combined therapy with reserpine, hydralazine and chlorothiazide was obtained, sufficient to alleviate the major symptoms.

CASE 2.—B.M., male, 12 years, complained of increasing headaches for eight weeks, associated with nausea, weight loss, blurred vision and nocturia. The blood pressure was 230/180 mm. Hg. Because of the absence of any history of significant past illness, the boy was thought initially to have an intracranial lesion. However, urinalysis revealed a marked proteinuria as well as granular casts and white cells observed by microscopic examination. *Staphylococcus albus* was cultured from the urine. Further studies revealed impairment of renal function, which, however, was not reflected by the surprisingly low value of the blood urea nitrogen, 22 mg. %. Subsequent therapy included salt restriction, reserpine, hydralazine and penicillin, and was associated with some improvement.

The findings in this patient emphasize the marked degree of hypertension which may occur despite only moderate apparent damage of kidney function. It is presently impossible to determine how much of the renal dysfunction is primary and how much secondary to the hypertension.

Unilateral renal disease usually requires surgical intervention, as in Case 3.

CASE 3.—H.M., female, 9 years, was admitted to hospital because of fever and vomiting, having suffered from intermittent abdominal discomfort and headaches for one year and polydipsia and polyuria for one month before admission. She had an elevated blood pressure, 200/170 mm. Hg, no retinopathy, only a trace of proteinuria, and occasional granular casts and cells in the urine. Although the blood urea nitrogen was elevated only to 25 mg. %, the failure of the intravenous pyelogram to demonstrate any dye in the left kidney was significant. A subsequent aortogram (Fig. 2c) failed to demonstrate any outline by dye of the arterial vasculature leading to the left kidney. Surgical removal of the left kidney revealed it to be of the Goldblatt type, infantile in size, with evidence of pyelonephritic changes on microscopic examination. Two months postoperatively the blood pressure remained elevated (180/120) but after one year it had fallen to 120/80.

Obstruction of a renal artery may cause hypertension with subsequent renal dysfunction (Case 4).

CASE 4.—E.T., female, 4 years, was admitted for investigation of intermittent vomiting, disorientation, polydipsia and frequency and urgency of voiding. These signs had commenced at the age of three years, at which time she was noted to have elevated blood pressure, 220/190 mm. Hg, intermittent proteinuria and urinary casts. A fluctuation of urinary findings from 4+ to negative suggested initially an intermittent obstructive lesion. However, aortography revealed a deformed left renal artery (Fig. 2b). Surgical correction of this was followed by a decrease in blood pressure to 130/65 mm. Hg within two weeks and disappearance of the previous symptoms.

Labile cutaneous vasomotor reactions may give the clue to a phæochromocytoma (Case 5).

CASE 5.—M.M., male, 1½ years, was admitted to hospital for investigation of vomiting which had begun two weeks earlier. The parents stated that the baby perspired frequently and occasionally showed a transient rash. Examination revealed an elevated blood pressure (200/120 mm. Hg) and inconstant proteinuria. On the basis of these findings, as well as direct observation of periodic sweating, blanching, and a blotchy red eruption of the skin, a benzodioxane test was done and interpreted as positive. A radiographic search for a phæochromocytoma revealed a mass in the right lower chest (Fig. 2d). At operation, a right extrapleural mass was removed. The pathologist, Dr. W. L. Donohue, reported this to be a ganglioneuroma. The patient has had no further signs or symptoms.

Endocrine dysfunction may be associated with hypertension (Case 6).

CASE 6.—L.B., female, 4 years, was admitted for investigation of recurrent convulsions over a period of four days and left abdominal pain of one day's duration. Examination revealed the presence of a florid facies, axillary and pubic hair, and a mass palpable in the left mid-abdomen, but no changes in the genitalia. An elevated blood pressure (200/150) and grade 1 retinopathy were present. Urinalysis revealed only a trace of protein. 17-Ketosteroid excretion was 14 mg. per day (normal, 1 mg. per day). The intravenous pyelogram revealed no localization of dye in the left kidney. Laparotomy disclosed an extensive carcinoma of the left adrenal with metastases to the left kidney and left renal vein.

May young children, like adults, have essential hypertension? It occurs very infrequently and the physician finds it difficult to know when the diagnosis is clearly established. The very term "essential" indicates "no known etiology".

CASE 7.—W.H., male, 4 years, was admitted to hospital for therapy of an upper respiratory infection. Although the mother had noticed a "fast pulse" and the boy had complained of occasional headaches for three months, the finding of an elevated blood pressure (220/180 mm. Hg) associated with gallop rhythm was unexpected. All subsequent investigations failed to clarify the etiology, except for the repeated finding of moderate elevation of urinary aldosterone excretion. Maximal hypotensive therapy (reserpine 1 mg. per day, hydralazine 300 mg. per day, and hexamethonium 200 mg. per day) failed to relieve the embarrassed cardiovascular state, although the blood pressure decreased to approximately 150/110 mm. Hg. Since surgical intervention was deemed necessary and since the increased aldosterone excretion suggested abnormal adrenal function, unilateral and later complete bilateral adrenalectomy was performed.

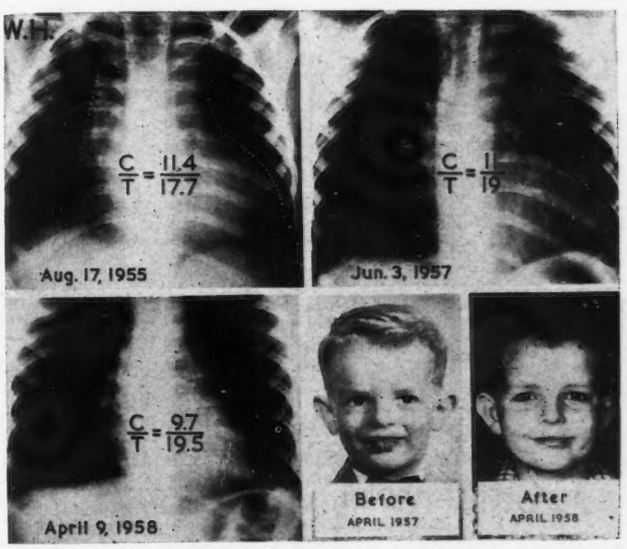

Fig. 3.—The hypotensive effect of bilateral adrenalectomy in Case 7 is revealed by the marked decrease in cardiac size: adrenalectomy was completed immediately after the radiograph of June 3, 1957. The alteration in facies of the boy is factual, though apparent change in the hair colour is a photographic artefact.

TABLE III.

Patient:	L.S., female	B.M., male	H.M., female	E.T., female	M.M., male	L.B., female	W.H., male	D.S., male
Age:	13.5 years	12 years	9 years	3 8/12 years	1.5 years	4 years	4 years	5 years
Chief complaint:	Headaches—3 years	headaches—8 weeks	Fever, vomiting	Polydypsia	Vomiting—2 weeks	Convulsions—4 days	Upper respiratory infection, cervical adenopathy	None
Symptoms and signs:	Headache incr. —6 months Fundi—grade 2 Femoral pulse present	Nausea Weight loss Blurred vision Nocturia Fundi—grade 2 Femoral pulse present	Headaches—1 year Abd. pain, pallor—1 yr. Polydypsia, polyuria—1 month Fundi—negative Femoral pulse present	Frequency of urination Headaches and convulsion—one occasion Hypertension, persistent proteinuria, casts, intermittent Fundi—negative Femoral pulse present	Periodic sweating, blanching and blotchy red rash Fundi—negative	Upperrespiratory infection Pain left abdomen—1 day Fundi—grade 1 L. abdominal mass Femoral pulse present Florid face Pubic, axillary hair Genitalia—no masculinization	Headaches and "fast pulse" 3 months Fundi—negative Gallop rhythm, large heart, femoral pulse present	None Fundi 0 Heart—normal Femoral artery palpable
B.P. (max.; min.)	228/172; 174/120	230/180; 200/160	200/170; 186/132	220/180; 155/130	200/120; 166/104	200/150; 160/130	220/180; 170/118	240/190; 180/150
Family history:	Maternal chronic ren. dis. and hypertension	Maternal uncle—nephritis	Negative	Negative	Negative	Negative	Maternal uncle—mild hypertension	None
Blood:								
B.U.N.	49-84	22.1	25.0	12.3	31 (N.P.N.)	22.0	13.0	16.7
Total protein		7.1	7.05	7.8			7.60	
Albumin		4.4	4.25	4.25			3.65	
Globulin		2.7	2.80	3.55			3.95	
Cholesterol		256.0		244.0			180.0	
E.S.R.	5		12.0	10.0	16.0		8.0	
Hb.	16.7	14.6	13.0	10.7	13.8	12.2	13.3	13.4
W.B.C.	9.4	9.0	10.0	4.6	8.2	11.4	23.8-8.0	6.0
Urine:								
S.G. (max.)	1.010	1.021	1.022	1.026	1.027	1.024	1.031	1.029
Protein	0—very faint trace	3+	Trace	0 - 3+	0 - 3+	Faint trace	0—trace	Trace
Sugar	0	0	0	0	0	0	0	Negative
Micro.	Rare W.B.C. and cell cast	Few W.B.C. and gran. casts	Occ. R.B.C., W.B.C. and gran. casts	0—numerous W.B.C. and occasional casts	Occ. W.B.C. and hyaline cast	0	Occ. hyaline cast Occ. W.B.C. and R.B.C.	0-cell casts
Culture	Negative	*Staph. albus*	*Strep. viridans* (light growth)	Ureters and bladder—negative	Negative	*Aerobact. aerog.* (contaminant?)	Negative	Negative
X-ray:								
Chest and heart	Negative	Negative	Negative; heart C/T—10/18.5	Negative; heart C/T—10/19.2	Heart C/T—9.2/17.8 3-cm. mass right C-P angle	Broncho-pneumonia	Heart boot shape; L.V.H.; R.A.H.	Heart negative. C/T = 9.9/19.8
Skull		Negative		Negative			Negative	Negative
I.V. pyelogram	No dye excretion	Left hydronephrosis	Impaired right kidney, no dye left kidney	Negative	Negative	No dye left kidney	Negative	Negative
Retrograde pyelogram	Dilated minor calyces	Negative	No left renal artery	Negative Constriction left renal artery		Displacement left kidney	Negative	Negative
Aortogram							Negative	Negative
E.C.G.:	L.V.H.	L.V.H.	L.V.H.	L.V.H.	L.V.H.	L.V.H.; R.A.H.	L.V.H.	L.V.H. (borderline)
Regitine (R); benzodioxane (B):	Negative (R)	Negative (R)		Negative (R)	Positive (B)	Negative (R)	Negative (R)	Negative (R)
Catechol amine excretion:		Negative	Negative	Negative			Negative	Negative
17-Ketosteroid excretion:				Normal		14.0 mg./day	Normal	1.6 mg./day
Serum electrolytes:	Na 141; K 4.1; Cl 112.	Na 143; K 2.9; Cl 94	Na 135; K 4.8; Cl 103	Na 144; K 4.2; Cl 99	Na 137; K 4.0; Cl 94	Na 135; K 3.7; Cl 106	Na 147; K 3.4; Cl 107	Na 136; K 4.6; Cl 99.5
Other tests:	Creatinine 2.9 Kidney G.F.R. 11; R.P.F. 68	Creatinine 1.0 Kidney G.F.R. 44; R.P.F. 260 L.E. cells 0	Aldosterone 10.6 μg./day Urea clearance 40%	Aldosterone 9.0 μg./day Creatinine and urea clearances normal Kidney G.F.R. 78, R.P.F. 250	Creatinine 0.7		P.B.I. 6.2 Aldosterone 12.6 μg./day Kidney G.F.R. 75; R.P.F. 380	Urea and creatinine clearance normal
Diagnosis:	Chronic pyelonephritis	Chronic pyelonephritis	Goldblatt syndrome of left kidney	Constriction left renal artery	Ganglioneuroma (phæochromocytoma)	Carcinoma of left adrenal; metastases left kidney and left renal vein	Essential hypertension	Essential hypertension
Treatment:	Reserpine, hydralazine chlorothiazide	Reserpine, hydralazine low salt diet, penicillin	Left nephrectomy (pyelonephritis)	Surgical repair (reserpine, hydralazine)	Surgical excision of extrapleural right paravertebral mass	Surgical removal tumour and left kidney	Reserpine, hydralazine, pentolinium tartrate; low salt diet; bilateral adrenalectomy	Reserpine and hydralazine
Response	Improved; no headaches Fundi—grade 1 B.P. 168/112	Improved; weight gain B.P. 148/108	2 months later—B.P. 180/140 1 year later—B.P. 120/80	Good B.P. 138/65; 125/80	Improved 3 years later—B.P. 120/80	No change; B.P. 150/100	Good—B.P. 110/88	Fair—B.P. 140/90 Remains asymptomatic

Legend and normal values

B.P.—blood pressure

Newborn	80/46
1 year	96/66
2 years	99/64
4 "	99/65
6 "	100/56
8 "	102/56
10 "	111/58
12 "	115/59
14 "	118/60

B.U.N. (blood urea nitrogen)—11-20 mg. per 100 c.c.
Serum total protein—7.0 g. per 100 c.c.
Serum albumin—4.0 g. per 100 c.c.
Serum globulin—3.0 g. per 100 c.c.
Serum cholesterol—150-250 mg. per 100 c.c.

Urine—S.G. (specific gravity)—1 027-1.030 (conc.).
—Protein—0 (80 mg. per 24 hours).
X-ray—C/T (cardiothoracic ratio) less than 50%.
L.V.H.—Left ventricular hypertrophy.
R.A.H.—Right auricular hypertrophy.

Serum electrolytes:
Na—Sodium 135-145 mEq./l.
K—Potassium—4.0-5.5 mEq./l.
Cl—Chloride—98-108 mEq./l.
P.B.I. (protein bound iodine)—3.5-8 μg./100 c.c.
Serum creatinine—up to 1.0 mg./100 c.c.

TABLE III.—*Continued*

Legend and normal values	Values adapted from (1). Variation of ± 10-20 mm. mercury can be expected within normal limits.	E.S.R.(erythrocyte sedimentation rate)—0-15 mm./hr. female 0-7 mm./hr. male Hb. (hæmoglobin)—12-15 g. per 100 c.c. W.B.C. (white blood count)—5000 cells/c.mm.	C-P Angle—Costo-phrenic angle. Catechol amine excretion—Urinary excretion (product of noradrenaline). 17-Ketosteroids—less than 1.0 mg./24 hr. before puberty Aldosterone excretion in urine—3-5 μg./24 hr. in children (Gornall method).	Kidney function: Creatinine clearance—a measurement of glomerular filtration rate (G.F.R.). 63-88 ml./min./-m². R.P.F. (renal plasma flow)—325-465 ml./min./m². Urea clearance—75-150%—normal.

The operative procedures were not attended by any difficulty, and both adrenal glands appeared normal. Subsequently the boy has been maintained on cortisone, 25-30 mg. per day, and salt-retaining hormone (9-α-fluorohydrocortisone), 0.05 mg. per day. Adrenalectomy has provided a decrease in blood pressure to approximately 110/85 mm. Hg and a return of cardiac size to normal (Fig. 3). Growth and development in the two years since operation have progressed normally, and the boy remains symptom-free and has a continued sense of well-being. A detailed report of the study and treatment of this child appears elsewhere.[12] The merit of this type of procedure must be viewed with the utmost caution, since it represents a form of therapy only to be considered after the most exhaustive investigations and the failure of all other forms of medical therapy.

CASE 8.—D.S., male, 4 years, was discovered to have hypertension (200/150 mm. Hg), during a routine health examination. All other additional investigations were negative, including an aortogram which is shown in Fig. 2a as the example of normal. On one occasion during investigation, when the blood pressure was recorded as 260/210 mm. Hg, the boy complained of headache and had some clouding of consciousness and a trace of protein in the urine. Therapy with reserpine, 0.75 mg. per day, and hydralazine, 75 mg. per day, has effected a decrease in blood pressure to 120-140/90-100. Chlorothiazide in doses up to 2 g. per day had no hypotensive effect. Since no untoward signs or symptoms are present, no further therapeutic measures have been taken. Periodic complete reassessment will be made in order to observe the appearance of heretofore undiscovered etiological factors; it must be classified at present as a case of essential hypertension.

SUMMARY

Problems of investigation and therapy of hypertension in children are reviewed, with special emphasis upon differential diagnosis.

Eight clinical examples are presented to illustrate the variegated clinical pictures which may be associated with hypertension.

Fig. 1 is reproduced (in altered form) from "Heart Disease in Infancy and Childhood" by J. D. Keith *et al.*, by kind permission of the authors and The Macmillan Company.

Fig. 2 is reproduced from *Pediatrics* (reference no. 12) by kind permission of the authors and the American Academy of Pediatrics.

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RÉSUMÉ

Par sa rareté, l'hypertension chez les enfants présente des problèmes particuliers dans le diagnostic et la conduite du traitement. La plupart des causes d'hypertension, comme les atteintes rénales ou endocrines et les lésions du système nerveux central, se retrouvent chez les enfants comme chez les adultes. Cependant l'hypertension dite essentielle est rare chez l'enfant et par contre, la coarctation de l'aorte et les tumeurs de Wilms sont relativement fréquentes. Les antécédents familiaux hypertensifs doivent mettre le clinicien aux aguets des adolescents dits "réactifs par hypertension". La tension normale s'élève graduellement d'environ 80/46 à la naissance jusqu'aux valeurs de l'âge adulte, atteintes à la puberté. Les auteurs indiquent leurs méthodes d'examen ainsi que certaines épreuves de laboratoire dans le dépistage de l'hypertension du jeune âge. Ils citent les noms de ceux qui ont récemment publié des rappels importants aux différents aspects du problème (Haggerty, McCrory, Yendt, Howard, Conn, Lewis, Genest).

La formule de thérapie se résume à la correction de la cause, et au traitement de l'hypertension même. En plus de l'intervention chirurgicale (s'il y a lieu) un certain régime de vie excluant les exercices violents peut être recommandé. Les diètes pauvres en sel ne sont généralement pas d'une application pratique chez l'enfant. Une combinaison d'hypotenseurs dosés d'après l'observation prolongée du malade, constitue la forme la plus sûre de thérapie. L'examen périodique du fond de l'œil, ainsi que des fonctions cardiaque et rénale s'impose au moins une fois par année. Les auteurs considèrent les poussées d'hypertension qui accompagnent quelquefois les néphrites hémorragiques aiguës comme des urgences médicales. Ils mettent en garde contre l'emploi intempestif du sulfate de magnésie et suggèrent comme alternative une combinaison de réserpine et d'hydralazine. Les données cliniques de huit cas d'hypertension chez des enfants sont présentées comme exemple.

HYPERTENSION IN ACROMEGALY

A study by Balzer and McCullagh (*Am. J. M. Sc.*, 237: 449, 1959) of levels of arterial pressure in 102 patients with acromegaly and one with gigantism demonstrated an increased incidence of arterial hypertension by the standards of Master, Dublin and Marks. By these criteria, hypertension was present in 34% of these patients as compared with 10% in a normal population. This hypertension was somewhat more common in women (37%) than men (26%); in four of five women less than 40 years of age, it was associated with symptoms of gonadal failure. No association could be established between hypertension and abnormal carbohydrate metabolism or increased serum phosphorus concentration.

It is concluded that acromegaly is not characteristically associated with hypertension, but that it may contribute to the development of hypertension in susceptible persons.

SOLITARY PULMONARY NODULE*

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THE DIAGNOSIS and management of the isolated pulmonary nodule present a challenge to the clinician. Mass x-ray surveys of the chest, originally intended to detect early pulmonary tuberculosis, have made it apparent that the solitary circumscribed pulmonary lesion is encountered rather frequently. Because the lesions are usually asymptomatic and because the radiologist can give little help, there is a tendency to delay the making of an exact diagnosis. Sharp and Kinsella[26] made exhaustive clinical studies in attempting to reach a correct diagnosis, but concluded that extensive investigations were not worth while. The high incidence of carcinoma in the reported series, along with the low mortality and morbidity associated with modern thoracic surgery, has changed the management and treatment of these lesions.

HISTORY

Graham and Singer reported a series of three cases of resected solitary pulmonary nodules in 1936, and Alexander, in 1942, recommended thoracotomy to establish a definite diagnosis in circumscribed lesions of the lung. Alexander emphasized the great frequency of malignant tumours in solitary pulmonary nodules. In 1947, Davis and Klepser[8] published a series of 40 surgical cases of solitary lesions of the lung, and in 1956 Davis and his colleagues[9] reported a total of 215 excised nodules, of which 47% were malignant neoplasms. Davis and Klepser, in a review of the literature, collected 1203 cases with a malignancy rate of 37%. Recently, a report from the Fitzsimmons Army Hospital, which is primarily a pulmonary disease centre receiving many cases from the areas in which histoplasmosis and coccidioidomycosis are endemic, showed a high incidence of granulomas (77%) and only 9.7% malignant lesions. The patients ranged in age from 17 to 74 years, approximately 70% being under 40 years of age.

Although many authors have reported their experiences with resected lesions, there have been only a few reports on the long-term fate of solitary lesions found in mass surveys. Holin,[14] in 1956, reported a five-year follow-up of 666 non-calcified solitary pulmonary nodules found on x-ray survey. In this group only 3.3% were untraced at the end of the five-year observation period, and in 74.7% no diagnosis had been established, but 11% of this group were suspected to be either tuberculous or carcinomatous. The incidence of malignancy was 3%, but on a second review of the cases there were 181 with calcification in the nodule which was not noted on the original roentgenogram. Thus, if this calcified group is excluded the incidence of carcinoma is 4.8%. Comstock, Vaughan and Montgomery[5] reported a smaller series of 88 cases followed up for an average of 53 months. In the 55 non-calcified lesions there were four carcinomas.

In Ontario, mass surveys are carried out by the Division of Tuberculosis Prevention under the direction of Dr. G. C. Brink.[3] Over 300,000 miniature chest radiographs are taken yearly and the abnormal findings are reported to the referring physician, with recommendation for further investigation. In 1953, a survey of the suspected tumour cases carried out by the Division on 312,941 miniature chest radiographs revealed 97 suspected tumours, of which 29 were solitary nodules. A questionnaire on the 97 suspected tumours showed that only 41 cases (42%) had had a further investigation and that of the 29 solitary lesions nine had had the diagnosis confirmed by surgical excision. In this group of nine patients three had granulomas, three had primary bronchogenic carcinomas, one secondary carcinoma and two benign tumours.

MATERIAL

This report is based upon 60 consecutive resections of solitary pulmonary nodules over a ten-year period, 1948 to 1958. The cases for study were treated at the Toronto Western Hospital and at Sunnybrook Hospital (D.V.A.). Patients ranged in age from 28 to 72 years.

TABLE I.—NUMBER OF CASES (60)

Primary carcinoma of lung	28 (47%)
Secondary carcinoma of lung	5 (8%)
Granulomas	22 (37%)
Benign tumours	4 (7%)
Loculated hæmatoma	1

The criteria for inclusion of the solitary pulmonary nodules were that the lesion must be: (1) round or oval in shape and measuring 1 to 6 cm. in diameter, (2) surrounded on all sides by lung, (3) homogeneous in density, (4) solitary, (5) without cavitation, (6) without conglomerate calcification or central core of calcification.

The lesion was frequently discovered on a miniature chest roentgenogram and confirmed by a 14 x 17 inch chest roentgenogram. In 26 cases planigraphy was done, and four had a bronchography and two a diagnostic pneumothorax. Bronchoscopy was carried out in 10 cases, with a positive cytological examination in two cases. As a general rule, bronchoscopy was not carried out in the peripheral lesions, because it was not usually helpful in establishing a diagnosis.

Table I shows that there were 28 (47%) primary malignant tumours of lung, which were treated by pneumonectomy in 10 cases, lobectomy in 17 cases and segmental resection in one case. Although there is much variation in the interpretation of

*From the Toronto Western Hospital.

cell types and patterns, the pathological reports in this group of cases showed 10 anaplastic or undifferentiated tumours, 8 epidermoid or squamous cell carcinomas, 8 adenocarcinomas and 2 alveolar cell carcinomas (Table II). Most of the patients were male, although there were nine females (32%), four of whom had adenocarcinomas and two alveolar cell carcinomas.

TABLE II.—PRIMARY CARCINOMA OF LUNG (28)

Anaplastic carcinoma	10 (36%)
Epidermoid carcinoma	8 (29%)
Adenocarcinoma	8 (29%)
Alveolar cell carcinoma	2 (7%)

Between 1948 and 1953, 11 resections were carried out for primary carcinoma of the lung. The five-year follow-up revealed that six patients had died, three could not be traced and two (18%) were alive and well. The two who survived for five years were men, one with an adenocarcinoma and the other with a squamous cell carcinoma. Overholt and Bougas[22] report a 40% five-year survival rate with resections of localized pulmonary cancer. A similar report by Ochsner, DeBakey and Dixon[21] gives a 42.9% five-year survival rate.

Of 28 patients with primary lung carcinomas 10 died within two years, and it was noted that the greatest mortality occurred within the first year after operation. This was probably due to undetected secondary deposits at the time of operation. In the 28 cases there was a high proportion (36%) of anaplastic carcinomas, and this probably influences the result, as the poor prognosis in this type of tumour is well known.

Of the 22 granulomas (37% of the total series) there was no definite proven lesion caused by a fungus. Cultures for tubercle bacilli and guinea-pig inoculation were carried out in 13 cases, and in six a positive result was obtained. Two of these cases were sent to the sanatorium for postoperative management with antimicrobial drugs. One patient was treated in the sanatorium for a year, after which he returned to work. The other patient was treated for six months and returned to work. The remaining four patients returned to work two to three months after operation, but were treated with antimicrobial drugs for six months postoperatively. There has been no recurrence of tuberculosis in these patients. It has been our practice to treat the granulomas with antimicrobial drugs postoperatively until the results of culture and guinea-pig inoculations are reported, but the patient is allowed to return to work in four to six weeks unless the lesion is frankly caseous. If tubercle bacilli are isolated from the lesion, antimicrobial drugs are continued for a total of six months while the patient is at work.

Of the five metastatic tumours, three originated from a hypernephroma, one from an osteogenic sarcoma and one from a melanotic sarcoma. The latter patient is still alive and well three years after pulmonary resection, and in addition one patient with a metastatic lesion from a hypernephroma is still alive. The patient with the metastatic tumour from the osteogenic sarcoma lived over three years after excision of the pulmonary neoplasm. The original tumour was excised from the right fibula in June 1951, and a segmental resection of the pulmonary lesion was carried out in September 1951. The patient subsequently died of his disease on October 26, 1954. Strieder[28] reported a series of 22 metastatic pulmonary lesions treated surgically. The best results were obtained in two patients with adrenocarcinoma of the fundus of the uterus, with survival times of 80 and 58 months, and in two patients with hypernephroma who survived 98 and 52 months. Kergin,[17] in 1954, reported nine cases with a survival of 6½ years (80 months) after excision of a metastatic lesion from a fibrosarcoma. In view of the fact that the pathway of extension in metastatic pulmonary tumours is less likely to be along lymphatics than in the primary disease, it has been stated that a lesser resection can safely be carried out.

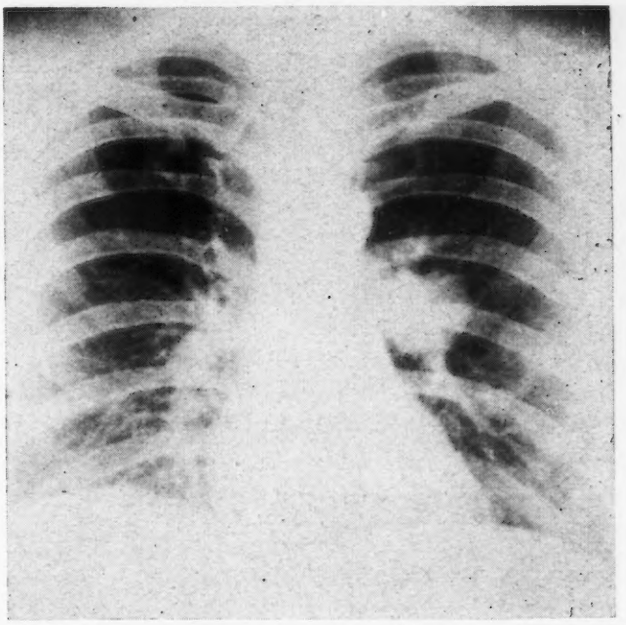

Fig. 1.—Chest roentgenogram of benign lymphoid tumour of left lower lobe.

Of the four benign tumours in the series there were two adenomas, one hamartoma and a case of localized hyperplasia of a lymph node situated close to the hilus of the left lower lobe. Castleman, Iverson and Menéndez[4] classified this latter tumour as "lymphoid hyperplasia resembling thymoma" and has collected 13 cases. The roentgenogram and photomicrograph of this benign lymphoid tumour are illustrated in Figs. 1 and 2.

In the entire group of 60 cases there was no mortality, and no serious complications were encountered. The morbidity was minimal and frequently the patient had returned to work in two to three weeks. A more conservative approach was adopted when the pulmonary nodule was frankly caseous and contained tubercle bacilli.

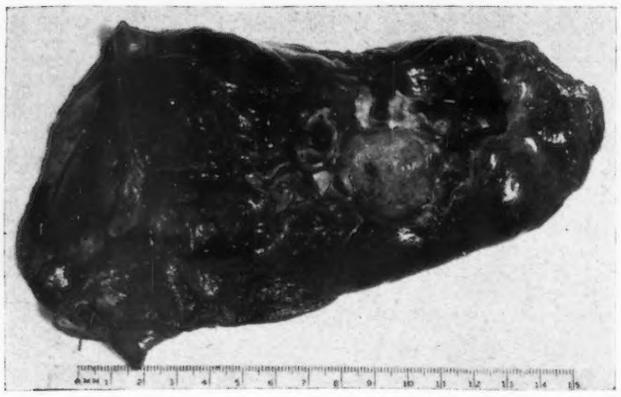

Fig. 2a.—Surgical specimen—left lower lobe with tumour close to bronchus.

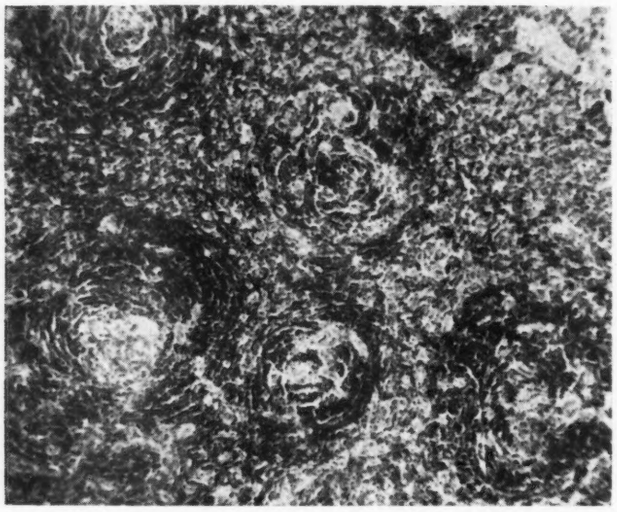

Fig. 2b.—Photomicrograph of benign lymphoid tumour. × 90.

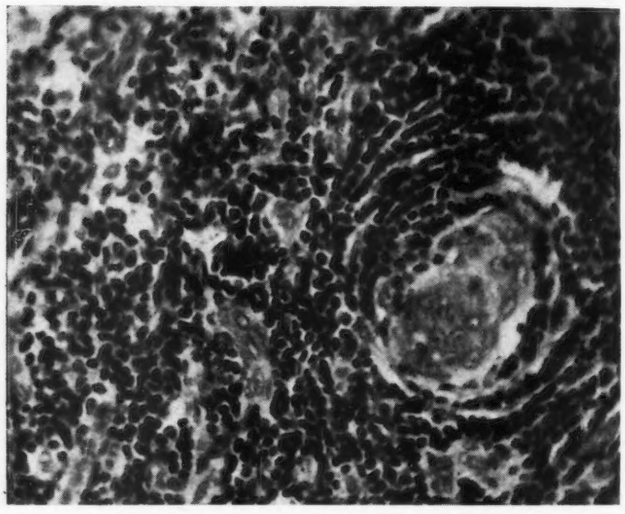

Fig. 2c.—Photomicrograph of benign lymphoid tumour. × 500.

DISCUSSION

Several factors may influence the selection of solitary pulmonary nodules for surgery. Although a large gamut of tests is available for diagnosis, the outstanding characteristic is the failure to establish a positive and confirmed diagnosis by any means other than thoracotomy. A history of previous malignant disease indicates the possibility of a metastatic lesion. Laminography or planigraphy may be helpful in making a diagnosis, as well as cytological examination of the sputum in some cases. The presence of calcification in the pulmonary nodule does not indicate a benign lesion. O'Keefe reported that 10% of solitary bronchial carcinomas show evidence of calcification, and this report was confirmed by a survey by Davis, who stated that the presence of minimal calcification within a solitary pulmonary nodule is unjustifiable grounds for assuming it to be benign. But if the lesion contains a relatively central core of calcification or concentric laminations, the lesion is probably benign and a more conservative approach is justified.

Among primary pulmonary malignant tumours, the adenocarcinoma is predominantly peripherally situated, and as a result appears to be more frequent in the reported series of solitary pulmonary lesions. This type of tumour appears to present a different pattern from the squamous and undifferentiated carcinomas and may be unrelated to smoking. It is relatively less uncommon in women and possibly in young people. The mode of spread is primarily by blood stream; if not removed, the tumour is more rapidly fatal, but if it is removed the prognosis is probably better.

Although the problem of dealing with the metastatic pulmonary nodule is difficult, the results of surgery are encouraging and appear to justify the continuation of pulmonary resection in selected cases for metastatic pulmonary disease. In a few cases the suspected malignant tumour may be a primary benign tumour or granuloma.

In most reported series in the United States the granuloma is the most common single entity among solitary pulmonary nodules. Fungus disease is not endemic in Ontario and appears to be uncommon in this particular area, although a series of cases of histoplasmosis has been reported in Eastern Ontario. Davis believes that many of the granulomas are indolent mycotic foci with either dead or dying fungi which can seldom be recovered by cultures and are generally invisible in tissue stained with hæmatoxylin and eosin. As a result, Davis advises the periodic acid-Schiff stain (P.A.S.) to identify the organisms.

Solitary lesions must be carefully investigated for tuberculosis, with cultures for tubercle bacilli and guinea-pig inoculation. In non-caseous granuloma, the patient is rehabilitated to his work in three to four weeks, but if tubercle bacilli are reported, the patient is allowed to continue work with antimicrobial drugs for a total of six months while at work.

It has been noted that many granulomas have been labelled as tuberculomas, and the patients have spent long periods under treatment for active tuberculosis. A positive diagnosis by culture or guinea-pig inoculation is indicated before pro-

longed treatment with antimicrobial drugs is necessary. Rich[24] avoids the term tuberculoma of the lung, and in a recent communication states that "the word tuberculoma is often used to designate a circumscribed microscopic tuberculous nodule, ordinarily largely or completely caseous. The term is loosely used—there is no particular size at which a nodule is called a tuberculoma rather than a tubercle, or a tuberculous nodule." The terms "focal tuberculosis" or "encapsulated tuberculosis" probably describe the condition adequately.

SUMMARY

The significance of isolated pulmonary nodules is reported with reference to a series of 60 surgically treated cases; the existence of a primary malignant tumour of the lung has been noted in 47% of these patients. There was no mortality or serious complications in this group. It is emphasized that no satisfactory criteria exist for the exact diagnosis of the solitary pulmonary nodule; in recent years, it has been noted that minimal calcification may occur in carcinoma of the lung. Certain patterns of calcification, however, suggest a benign lesion, and in this group a more conservative approach may be adopted.

Lobectomy appears to be an adequate cancer operation in properly selected cases, both with primary and with metastatic tumours. The risk of exploration and excision of asymptomatic nodules is slight and the risk of delay is often great.

Full investigation of granulomas is required and the term "focal tuberculosis" or "encapsulated tuberculosis" is suggested for the isolated lesions in which tubercle bacilli are demonstrated.

The physician is responsible for investigation and correct management of isolated pulmonary nodules. The significance of the abnormalities, the inadequacy of diagnostic methods and the danger of procrastination are emphasized. With few exceptions, isolated intrapulmonary nodules are best treated by prompt surgical exploration, unless an exact preoperative diagnosis is possible, or a malignant tumour can be excluded with certainty.

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RÉSUMÉ

L'importance d'un nodule pulmonaire isolé est mise en évidence dans une série de 60 cas de chirurgie par la découverte chez 47% d'entre eux d'un carcinome primaire du poumon. Tous les malades supportèrent bien l'intervention. On fait remarquer qu'il n'existe aucune manière satisfaisante d'arriver à un diagnostic précis du nodule pulmonaire isolé. On a récemment remarqué qu'une légère calcification peut se produire dans les cancers du poumon. Certaines formes particulières de calcification laissent entrevoir une lésion bénigne de sorte qu'une attitude plus conservatrice peut être adoptée dans ces cas. La lobectomie semble constituer une intervention satisfaisante dans des cas choisis tant de lésions primaires que métastatiques. Les risques que comprennent l'exploration et l'excision d'un nodule silencieux sont légers alors que ceux que comportent la tergiversation peuvent être lourds de conséquences. Les granulomes doivent être soumis à une enquête minutieuse. L'auteur suggère les termes "tuberculose focale ou encapsulée" pour décrire les lésions isolées contenant du B.K. La conduite à tenir en face des lésions pulmonaires isolées à forme nodulaire consiste en une exploration chirurgicale immédiate à moins qu'on ne soit arrivé à un diagnostic pré-opératoire exact ou qu'on ait éliminé avec certitude toute possibilité de cancer.

CARCINOMA OF THE FLOOR OF THE MOUTH

Carcinoma of the floor of the mouth is uncommon, and a review by MacFee (*Ann. Surg.*, 149: 172, 1959) of clinical observations and treatment is useful, for the condition is easily recognized and operable if treated reasonably early. Recently the role of tobacco and slaked lime as an etiological factor is emphasized over the betel nut in India, where it is common. Leukoplakia, vitamin B deficiency, and syphilis are still regarded as factors. It is an epidermoid or squamous-cell cancer and spreads by direct extension and to local lymph nodes more frequently than by blood stream, and nodes are involved in over 50% of cases. Often the glands on the opposite side of the neck show metastases.

Symptoms are not severe till late: a swelling in the neck, stiffness in moving the tongue, difficulties in enunciation, pain in the ear, a stinging sensation, deviation of the outthrust tongue, or an ulceration. A good biopsy specimen is easily obtained.

Treatment by irradiation, especially of the lymphatic metastases, has fallen short of expectation. Surgical excision is increasingly popular in cancer centres, and operations for small and advanced growths, with and without resection of a portion of the mandible, tongue, and radical dissection of the cervical lymph nodes, are described. The problem of the indications for block dissection of the neck, and of the opposite side especially, is discussed.

The results of treatment of cancer of the floor of the mouth seem to be improving over the years. Five-year survivals of one-third of the patients without clinical metastases and of one-sixth if metastases are present may be expected. Including all cases in a large group, one-quarter are well five years after diagnosis.

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THE CRYSTALLIZATION OF CERVICAL MUCUS
A CRITICAL ANALYSIS BASED ON CLINICAL RESEARCH

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All parts of the female generative tract undergo cyclical changes, and it has long been known that physical and chemical variations occur in the cervical mucus and that these variations are related to the menstrual cycle. The cyclical changes occurring in cervical mucus were first reported by W. Tyler Smith in 1855. He stated that the mucus was thin and viscid in the weeks following the menstrual period. Seguy and Vimeux[1] noted that for several days in mid-cycle, at about the time of ovulation, the cervical mucus becomes more translucent and less viscid while the cell count is low or absent. Seguy and Simonnet[2] established that the physical changes in the cervical mucus were associated with œstrogen secretion. The increase in cervical mucus secretion may be noted in post-menopausal women who are on œstrogen therapy.

Palmer[3] studied the action of hormones on castrated women, and observed that the secretion of mucus is stimulated by œstrogens and inhibited by progesterone. Abarbonel[4] studied a group of women who had had a subtotal hysterectomy and bilateral oophorectomy, and was able to produce the cyclical physical variations in cervical mucus by cyclical administration of œstrogen and progesterone. Viergiver and Pommerenk[5] studied the quantitative variations in the amount of cervical mucus secreted during a cycle. They showed the variation to be from 60 mg. just after the period to 200 to 700 mg. for about four days in mid-cycle and then 60 mg. in the later part of the cycle. They also observed that the increase in cervical secretion comes one to three days before the rise in the basal body temperature. Papanicolaou[6] in 1945 described the crystals which are formed when a drop of cervical mucus is placed on a slide and allowed to dry. This characteristic crystallization was also described by Rydberg and Madsen[7] in 1948. Rydberg also reported the chemical composition of the crystals. The crystals were found to be common salt, and the crystal formations were due to the presence of mucin. Zondek[8] has shown that the crystallization is not specific for cervical mucus because the same phenomenon appears in all mucus secretions and most body fluids. Londerstromland, a co-worker of Rydberg, analyzed cervical mucus as follows:

Total amount of cervical secretion ...	365.3 mg.
Dry matter	5.9 mg.
Ash (total)	3.1 mg.
Organic matter	2.8 mg.
Chloride as NaCl	3.0 mg.

The presence of electrolytes, proteins and carbohydrates is indispensable for crystallization. The crystal structures can also be produced by drying a drop of salt solution to which protein has been added.

The cervix is lined by tall, columnar epithelium. Racemose glands dip down from the mucosa of the endocervix into the fibromuscular stroma of the cervix. The glands secrete mucus. The continuous production of mucus normally prevents the entry of harmful organisms into the cervical canal.

Cyclical changes associated with crystallization of cervical mucus are related to the secretion of œstrogen and progesterone, as are the cyclical changes in the physical character of the mucus. Crystallization is favoured by œstrogen and inhibited by progesterone. These observations have been verified by Campos Da Paz,[10] Roland,[11] Zondek[8] and others. Since the papers of Campos Da Paz and Roland, many papers have shown the value of cervical mucus study in assessing the time of ovulation and the receptivity of the mucus to the sperm, in the diagnosis of pregnancy, and in the estimation of placental insufficiency. We have found some of these observations to be true, but with some of the observations we disagree. This paper is a critical assessment of the clinical value of observation of the crystallization phenomenon of cervical mucus. The experience and observations made in this study have been gained primarily from patients in private practice. We have also gained experience from the teaching patients in Victoria Hospital, London, Ontario; and the gynæcological clinic of the University Hospital, Ann Arbor, Michigan.

TECHNIQUE OF MAKING THE SMEAR

The method of examination of a cervical mucus smear is very simple and because of its simplicity is an office procedure. The cervix is exposed with a dry speculum and the surface is wiped with a cotton sponge.

Various means of collecting the mucus have been described and are shown in Fig. 1. The materials used for collection are a cotton-tipped applicator, a wire loop as used in bacteriology, and a 13-gauge 4-inch spinal needle which has had the tip squared off. Attached to the needle is a 10 c.c. Luer-Lok syringe for applying suction. We originally used the syringe and needle. Because of the difficulty of obtaining scanty or thick mucus with it, we have found the most satisfactory means of collecting the mucus to be the cotton-tipped applicator. The applicator is inserted about 1 cm. into the cervical canal and rotated several times. The mucus so obtained is deposited by rolling the applicator on a clean, dry slide. The smear should

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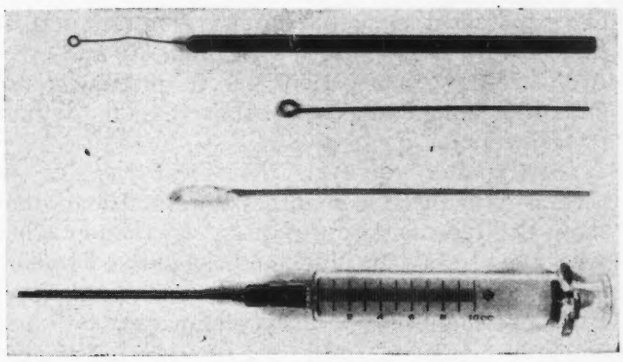

Fig. 1.—Equipment which may be used to collect cervical mucus.

be a thin one. The mucus on the slide is dried quickly and thoroughly over any convenient source of heat such as a lamp or radiator. The smear thus made can only be preserved for a period of several months. After that time there is destruction and degeneration of the crystals.

Small amounts of blood in the mucus, as found in threatened abortion, or a marked cervicitis will interfere with the interpretation. The crystals do not form to their fullest extent in the presence of even small amounts of blood.

INTERPRETATION OF THE SMEAR

Two general classifications for the interpretation of the smear have been suggested. Both of these are quantitative to some degree, because they depend to a certain extent on estimating the amount of crystallization present in the smear. The one developed by Campos Da Paz divides the smear into four types:

Classification of Campos Da Paz:

1. *Negative*: The smear shows no evidence of crystallization. There are only round, clear mucous globules and usually some cells (Fig. 2).

2. *Atypical*: The smear shows some tendency to crystal formation although the pattern is not clear. There may be some crystals which are thick and ragged. Many areas of the field may show mucous globules and cells (Fig. 3).

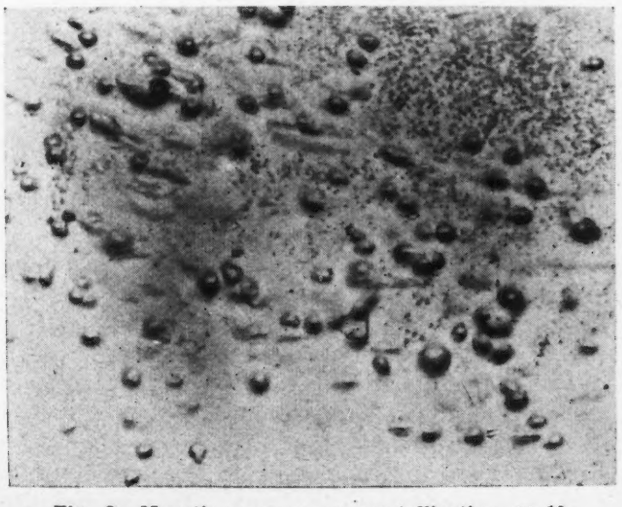

Fig. 2.—Negative smear, no crystallization. × 10.

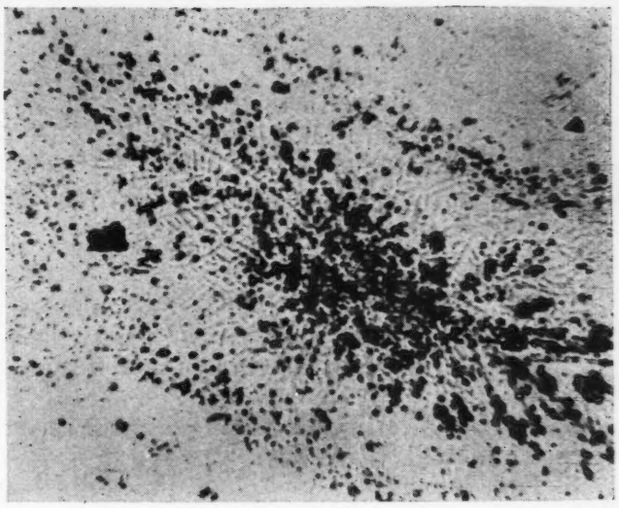

Fig. 3.—Atypical smear. There is some slight suggestion of crystal formation. × 10.

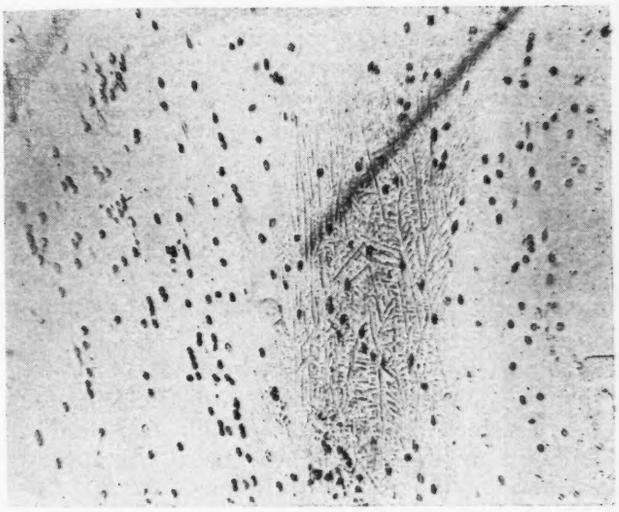

Fig. 4.—Partial typical crystallization. There is some typical crystallization in one area of the smear. × 10.

3. *Partial Typical*: Some areas of the smear may show a small number of typical crystals. In other areas there will be atypical or negative crystallization (Fig. 4).

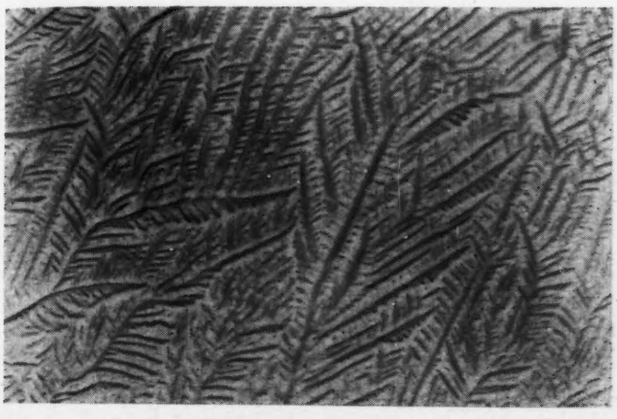

Fig. 5.—Typical crystallization. × 10.

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4. *Total Typical Crystallization*: The whole field in any section of the smear shows the typical, delicate, fern-like pattern of crystallization (Fig. 5). At the edge of the smear there may be some areas of no crystallization because of the thinness of the smear.

Zondek has tried to introduce a more quantitative estimation into his interpretation.

Classification of Zondek:

1. *3 plus* – strongly positive reaction, with most of the dried mucus in any field in a state of typical crystallization.
2. *2 plus*–typical crystallization present in several places in a field.
3. *1 plus*–typical crystallization present in only a few places.
4. *Negative*–no typical crystallization.

The various classes of the above classifications compare to some degree with one another.

We do not feel that this test lends itself to either the classification of Campos Da Paz or the quantitative evaluation advocated by Zondek. The amount and character of crystallization in the smear are influenced to some degree by the thickness of the smear. It is impossible to have smears of equal thickness. After all, the whole question of interpretation depends on whether there is complete crystallization throughout most of the body of the smear, which apparently indicates that œstrogen production is high; or whether there is no crystallization at all, which means that some change has taken place, apparently progesterone production, which inhibits the crystallization.

In our study we have not been able to estimate the amount of crystallization in the field in quantitative fashion. Since there are only two significant findings in the smear, we have classified our readings of the smear as follows:

1. *Positive*–total and typical crystallization in the whole field and over the whole slide except possibly at the edges of the smear.
2. *Negative*–there is not total typical crystallization. This would include Groups 2, 3 and 4 of the other classifications.

MUCUS CRYSTALLIZATION THROUGH THE MENSTRUAL CYCLE

1. *Ovulatory Cycle.*

After the menstrual period has ceased, there is no crystal pattern to the smear. The mucus obtained is scanty, and the dried smear shows only streaks and globules with usually some vaginal and cervical epithelial cells. Within a day or two a crystal pattern can be recognized in parts of the smear and there is an absence of cells. As mid-cycle is approached, the cervical mucus becomes more abundant, clearer and thinner, and the crystallization pattern on the dried smear becomes more intense. The pattern of crystallization is described by Campos Da Paz and Roland as akin to the palm leaf, or simple ferning. Zondek describes that picture as one of arborization. At mid-cycle in the 28-day cycle patient, the ferning is intense and the complete smear shows total, typical crystallization.

Shortly after mid-cycle the smear changes. In several days there is a mixed pattern. Some areas show the typical crystal pattern whereas in other areas the crystals are thick and ragged and broken up, or there may be no crystals at all. As the end of the cycle approaches, the crystal pattern becomes much less marked until, a few days before the end of the cycle, there is no evidence of a crystal pattern and the smear shows only a dense globular pattern intermingled with vaginal and cervical epithelial cells.

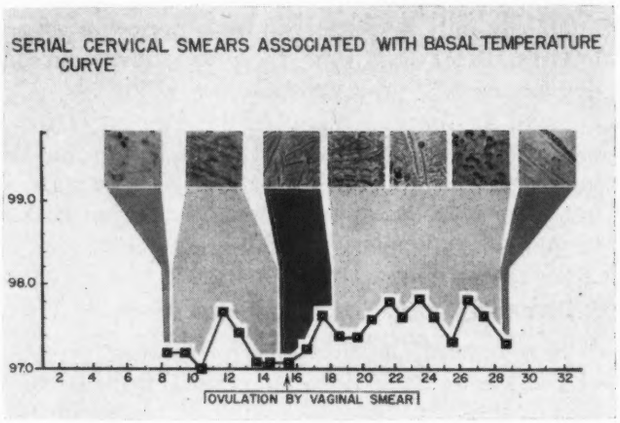

Fig. 6.—Changes which occur in cervical mucus smear, basal body temperature and vaginal smear during a normal cycle.

Early in this study we followed up a series of 24 patients with cervical smears every other day, basal body temperatures and vaginal smears. Fig. 6 shows the typical findings. The stage at which the various changes occur in the cycle varies with each patient. The most pronounced changes occur gradually between the 10th and the 22nd day in the patient with a 28-day cycle. For practical purposes it is only necessary to study the smear over this 12-day period.

2. *The Anovulatory Cycle*

Little has been written of the findings in the anovulatory cycle. Campos Da Paz[9] states that in the anovulatory cycle typical crystallization appears in the second half of the cycle when there is a normal œstrogen level and a cervical glandular epthelium showing normal response to the hormonal stimulus. Roland[10] states that in the anovulatory cycle the cervical mucus smear shows persistent "fern-like" structure up to the onset of bleeding.

Our findings do not agree with those described by the above authors for the anovulatory cycle. In the patients whom we have studied there has been a typical crystal pattern at mid-cycle but there has been an abrupt change to a negative smear within a period of 48 hours. The anovulatory

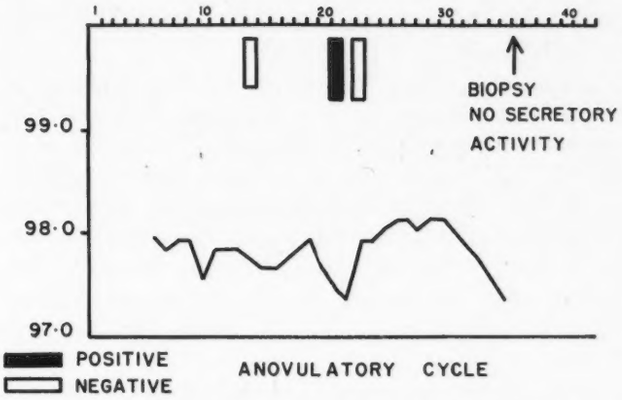

Fig. 7.—Changes which occur in the cervical smear and basal body temperature during an anovulatory cycle.

cycles which we have studied have occurred in infertile patients and have been verified by an endometrial biopsy taken on the first day of the period. Fig. 7 is an example of the changes found in the patient with an anovulatory cycle. This patient had a 34-day cycle. The smear was positive on the 20th day and there was an abrupt change to a negative smear on the 22nd day. Fig. 8 is a photomicrograph of the endometrium of the same patient taken on the first day of the menstrual period.

We do not know why there should be a difference in findings in the anovulatory cycle. We would like to suggest, however, that the cyclical changes which occur in cervical mucus are due to quantitative variation in œstrogen level rather than to an œstrogen-progesterone relationship.

THE CERVICAL MUCUS SMEAR IN PREGNANCY

We have studied the cervical mucus smear in 200 patients known to be pregnant. The duration of the pregnancy when the smear was taken varied from 3 to 36 weeks. One smear was positive and 199 smears were negative. Among the negative smears there were 120 showing some attempt at crystallization.

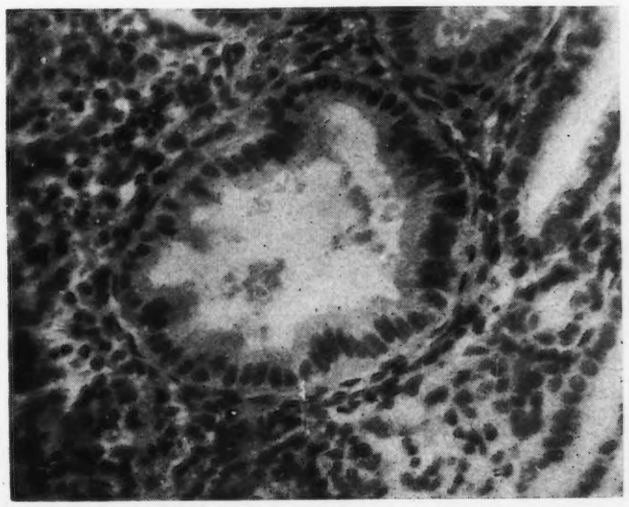

Fig. 8.—Photomicrograph of an endometrial gland during an anovulatory cycle. × 6.

During pregnancy the mucous plug is gelatinous and the mucus is difficult to obtain. The usual pattern is a cellular smear mixed with threads of mucus which may show some attempt at crystallization. The lack of crystallization during pregnancy is said to be due to a persistence of the corpus luteum and a high progesterone level in spite of the high œstrogen level which is also present during pregnancy.

Fig. 9 shows the findings in a patient undergoing infertility studies who became pregnant.

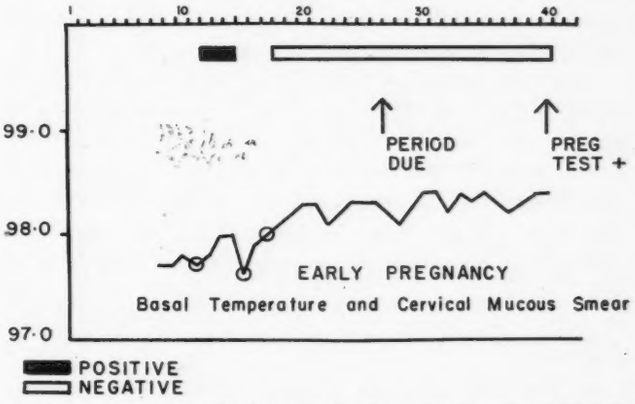

Fig. 9.—Changes which occur in the cervical mucus smear and the basal body temperature with the advent of pregnancy.

Zondek and Cooper[12] state that in pregnant women typical crystallization cannot be achieved even with high doses of œstrogen. In our study of pregnant patients the one patient in the series whose smear showed typical crystallization on a number of occasions was in early pregnancy and was receiving 5 mg. stilbœstrol three times daily. This patient carried on to term and delivered uneventfully. We would like to suggest that abnormally high levels of œstrogen will inhibit crystallization, as does progesterone.

Six patients in this series showed partial typical crystallization. They were between 17 and 30 weeks of pregnancy and none had any complications. In this group of 200 patients there were 128 in whom the smear was taken before the 14th week. Of this group eight aborted, and seven of these had a completely negative smear. In the patient who aborted there was some suggestion of crystallization in the smear. The patient was 10 weeks pregnant. At the time of dilatation or curettage of the uterus there was no evidence of a fetus.

In the Diagnosis of Pregnancy

Roland[10] and Sprague[11] advocate the use of cervical mucus smears as a simple and rapid test for pregnancy in its earliest stages. They base their findings on the fact that in pregnancy there is no true crystallization. Zondek and Cooper[12] use the cervical mucus smear in the diagnosis of pregnancy but in a somewhat different manner. They gave 50 women in early pregnancy 10 mg.

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of œstradiol benzoate intragluteally. In 49 of these patients arborization of the cervical mucus did not occur after four days. On the other hand, they feel that if a woman misses a period because of functional amenorrhœa the crystallization of cervical mucus can be achieved with œstrogen.

We have studied 50 patients in whom we were only concerned with the diagnosis of pregnancy. The mucus smear was obtained and read before pelvic examination was carried out. The presence or absence of pregnancy was confirmed by the frog test or subsequent follow-up of the patient. A correct diagnosis was made from the smear in 86%, while a false positive test was given in 14%.

Because many pregnant patients may show some degree of crystallization, we considered that to be sure that a patient was pregnant there must be no crystallization. In our hands we do not consider that this test shows sufficient accuracy for it to replace the recognized pregnancy tests. The use of the cervical mucus smear in conjunction with a history and pelvic examination may help to make the physician a little more certain of his diagnosis.

If the smear shows typical total crystallization, one can be sure that the patient is not pregnant. If the smear is completely negative, and if the findings in the patient suggest pregnancy, the cervical mucus smear may be used as corroborative evidence of pregnancy.

THE CERVICAL MUCUS SMEAR AT THE MENOPAUSE

Because of the cessation of ovarian function at the menopause there is no crystal pattern whatever and the smear shows only a loose pattern of cells. When a menopausal patient is on œstrogen medication, the smear will show some crystallization if the dose of œstrogen is sufficient to relieve the symptoms. The mucus smear may thus be used as a means of testing the effectiveness of œstrogen therapy in the menopausal patient. The cervical mucus smear may be an aid in determining the type of medication which a postmenopausal patient is taking. We have seen two patients with postmenopausal bleeding who were taking pills, one believed for asthma and the other for headaches. Cervical mucus smears in both these patients showed typical mucous crystallization, and it was suspected that the medication which these patients were taking was an œstrogen preparation. Subsequent dilatation and curettage on these patients showed an œstrogenic type of endometrium, and it was later determined that these patients were taking œstrogen pills.

RECEPTIVITY OF CERVICAL MUCUS

At the time of ovulation the cervical mucus is greatest in amount, is clear and watery and shows the property of "Spinnbarkeit", that is, the cervical mucus may be stretched between two slide coverslips to a distance of about 12 cm. At the same time a cervical mucus smear shows maximal typical crystallization.

Sometimes, when following up the smears in a patient throughout a cycle one will see the crystallization pattern develop at the time of ovulation, but it will not be a truly typical pattern (Fig. 10). The physical changes in the mucus for ovulation will not be maximal. Unless crystallization is typical with maximal physical changes, the mucus may be hostile to the sperm attempting to penetrate it. The patient with this type of mucus will have a poor Huhner test.

The insufficient change in the mucus is due to some deficiency in œstrogen production. Campos Da Paz has shown that 5 mg. of stilbœstrol given on the 5th and 10th days of the cycle will improve crystallization and also the receptivity of the mucus. Behrman[13] has used 0.5 mg. of stilbœstrol daily from the 5th to 10th day of the cycle in order to improve receptivity of the cervical mucus.

We have used both methods on infertile patients but prefer stilbœstrol as advocated by Campos Da Paz. This does not appear to lengthen the cycle, whereas the Behrman method does. Of six patients who had hostile mucus, four have become pregnant with the use of 5 mg. of stilbœstrol on the 5th and 10th days of the cycle.

DISCUSSION

The cyclical crystallization which cervical mucus undergoes is a picturesque phenomenon. The cyclical changes are associated with the ovary and in turn with the secretion of œstrogen and progesterone. These changes do not occur in the absence of the ovary, but can be brought about by cyclical administration of œstrogen and progesterone. The crystallization is most typical at the period when œstrogen production is greatest and at the time when the mucus is most receptive to the sperm. After this period, progesterone inhibits the crystallization picture. The changes which occur indicate that ovulation has taken place. However, in four of these patients studied by us cervical mucus has shown the typical changes associated with ovulation but the endometrial biopsy has shown no secretory activity. We feel that this discrepancy may be due to several factors:

1. Zondek has shown that salt in any form on the needle, syringe or slide may cause crystallization, and he suggested boiling all equipment in distilled water.

We have attempted to show crystallization in our chemically softened water when mixed with protein and have been unable to do so. We therefore feel that the equipment is not responsible for these results.

2. The crystallization which occurs may be due to some quantitative variation in hormone production rather than to a direct œstrogen-progesterone relationship. Most authors have noted that crystallization following ovulation does not disap-

pear suddenly but does so gradually and is usually not complete until seven to eight days after ovulation. In the anovulatory cycles which we have studied there is a subtle change from crystallization to a negative smear in a matter of 48 hours. The change which the mucus smear shows may thus be due to a change in the level of œstrogen. A high level of œstrogen may cause crystallization, but a higher level, at least in the anovulatory cycle, may inhibit crystallization.

In using this procedure to detect ovulation one must at least combine its use if possible with study of basal body temperatures, vaginal smears and an occasional endometrial biopsy. During the time that ovulation is suspected, the smears should be taken daily for a week. If the change from a positive smear to a negative one is gradual, the presence of ovulation may be anticipated. If the change from a positive to a negative smear is sudden, one should suspect that ovulation has not occurred and an endometrial biopsy should be done.

The use of the cervical mucus smear in the diagnosis of pregnancy will not take the place of the usual well-known tests because of its inaccuracy, especially when the smear is negative. However, if a positive smear is obtained, one can be assured that the patient is not pregnant.

Perhaps the greatest use of the cervical smear is in the study of the receptivity of mucus to the sperm. For the mucus to be receptive it must be clear and watery and show "Spinnbarkeit". Receptive mucus also shows total and typical crystallization. If these properties are not present, they can be produced by giving the patient a modest dose of an œstrogen preparation on the 5th and 10th days of the cycle.

SUMMARY

Cervical mucus, when smeared on a slide and dried quickly, shows a typical pattern of crystallization at the time when œstrogen production is greatest during the cycle. The pattern changes to a negative one in the second half of the cycle. The change may be due to the production of progesterone or a change in the level of œstrogen.

In the ovulatory cycle the change is a gradual one occurring over a period of seven or eight days.

In the anovulatory cycles studied by us the change from a positive to a negative smear was an abrupt one, taking place within 48 hours. This sudden change may be due to a sudden and abrupt change in œstrogen level.

In pregnancy the smear is negative in most cases. Occasionally there may be some attempt at crystallization. There is no relation between crystallization and the tendency to abortion. The use of the cervical mucus smear as a means of diagnosing pregnancy is not sufficiently accurate to replace other well-known methods. However, if the smear shows typical and total crystallization, the patient is not pregnant.

The use of the cervical mucus smear is of most value in the study of the infertile patient. The typical pattern of crystallization must be present for the mucus to be receptive to the sperm. Hostile mucus can be made receptive by using 5 mg. of stilbœstrol on the 5th and 10th days of the cycle.

The smear in the menopausal patient is a negative one unless the patient is taking an œstrogen preparation.

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RÉSUMÉ

La glaire endo-cervicale lorsque étalée sur une lamelle et séchée rapidement présente une formation cristallisée typique, au sommet de la phase folliculaire. Cette image disparaît au cours de la deuxième moitié du cycle. Le changement peut être le résultat de la production de progestérone ou d'un abaissement du taux d'œstrogènes. Dans le cycle ovulatoire ce changement s'effectue graduellement au cours d'une période de sept à huit jours. Dans les cycles anovulatoires nous avons observé un changement brusque du positif au négatif en 48 heures. Ce changement soudain semble refléter un changement également brusque du taux d'œstrogène. Pendant la grossesse les étalements sont la plupart du temps négatifs. Quelquefois peut-on observer quelque ébauche de cristallisation. Il n'existe aucun rapport entre la cristallisation et la tendance à l'avortement. L'appréciation de la cristallisation de la glaire dans le diagnostic de la grossesse n'est pas assez précise pour remplacer les autres épreuves mieux établies dans ce domaine. On peut cependant affirmer que s'il y a cristallisation totale et typique la femme n'est pas enceinte. C'est dans l'étude de l'infertilité que cette méthod rend les plus grands services. La formation caractéristique doit exister pour que la glaire accepte le sperme. Une glaire réfractaire peut être rendue propice par l'administration de 5 mg. de stilbœstrol au cinquième et au dixième jour du cycle. Dans la ménopause l'étalement est négatif à moins que la femme ne reçoive des œstrogènes.

EFFECT OF GLUCAGON ON GASTRIC SECRETION IN MAN

The effect of glucagon on gastric secretion was studied by Janowitz (*Gastroenterology*, 36: 580, 1959) in 13 patients with ulcer diathesis and 11 patients with active gastric or duodenal ulcer. After intravenous injection of 2 mg. of glucagon, gastric and duodenal juice was obtained in divided specimens for five hours. All patients showed rises of at least 40 mg. % in the glucose level in their blood for about two hours, indicating a definite response to glucagon. In all of the patients with or without ulcer the result of intravenous glucagon injection was an inhibition of gastric flow, of secretion of acid and of pepsin. This inhibition persisted for at least five hours—that is, well beyond the period of hyperglycæmia. The authors conclude that glucagon is not a gastric stimulant and is unlikely to have ulcerogenic activity.

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MALABSORPTION SYNDROME FOLLOWING EXTENSIVE RESECTION OF THE SMALL INTESTINE*

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RECENT REPORTS have indicated that survival is not unusual after resection of all the small intestine distal to the proximal three feet (90 cm.) of jejunum.[1] The case to be reported falls within this group and is considered to be of special interest because of the striking improvement in undernutrition and convulsions after an alteration of the jejuno-colic anastomosis. This alteration eliminated two blind pouches and exposed all remaining small and large bowel to the intestinal contents. A unique finding in this patient just before the change of his anastomosis was the increased serum phosphate concentration in conjunction with marked hypocalcæmia, a combination which suggested the presence of hypoparathyroidism. The recent increase in steatorrhœa following discontinuation of intramuscular cortisone, oral sulfisoxazole and a gluten-free diet was also noteworthy.

The patient, a 19-year-old Dutch male labourer, was thrown from an automobile and sustained severe injuries to the small bowel and abdominal wall on July 8, 1956. Fig. 1 indicates the small bowel resection and anastomosis which was performed at that time. The ileum was removed along with all but the proximal 2½ to 3 feet (75-90 cm.) of jejunum. A jejuno-transverse colic anastomosis was made, leaving a blind jejunal loop of about 8 inches (20 cm.) beyond the anastomosis and diverting the intestinal contents from the proximal half of the colon.

During the next five months the patient developed steatorrhœa and diarrhœa with the passage of eight to nine foul bulky stools per day. He sustained a weight loss of 80 lb. despite a very large caloric intake. He developed signs of tetany followed by convulsions about one month before his admission to the Victoria General Hospital in December 1956. Fig. 2 shows his appearance at the time of admission. The marked undernutrition and the defect in the abdominal wall are obvious. Table I shows pertinent laboratory data obtained at that time. A very slight normocytic anæmia was present. The hypocalcæmia and hyperphosphatæmia were accompanied by an alkaline phosphatase level above the normal upper limit of 8.5 units per 100 ml. Several subsequent values of phosphatase were within normal limits, however. Radiographic bone studies did not show evidence of significant demineralization.

Oral and intramuscular calcium therapy along with large doses of vitamin D resulted in very little improvement in the serum calcium level, and even intravenous injections of calcium failed to control convulsions on some occasions. The serum phosphate level fell to 2.6 mg. per 100 ml. after exhibition of vitamin D, although subsequent values obtained while this agent was continued proved somewhat variable. The patient also received intramuscular injections of parathyroid hormone with slight or no effect on the serum calcium level or muscular irritability.

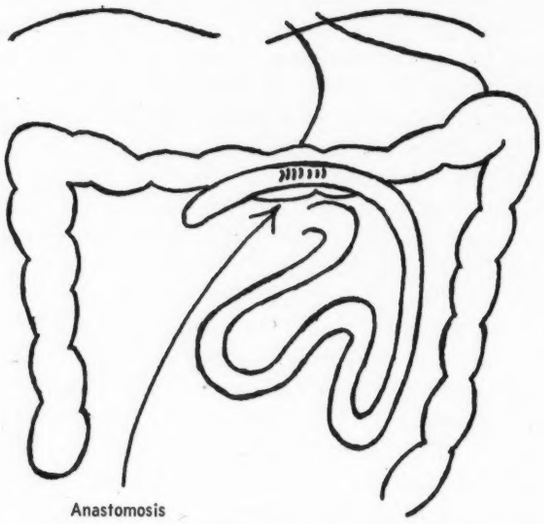

Fig. 1.—Diagram showing initial jejuno-transverse colic anastomosis.

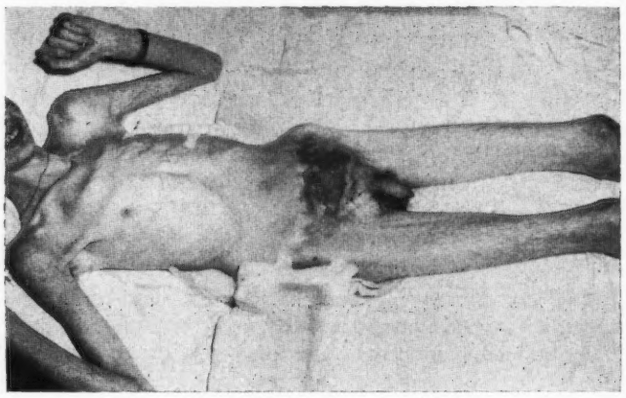

Fig. 2.—Patient's appearance in December 1956.

On January 28 (almost seven months after the injury) Dr. E. P. Nonamaker replaced the jejuno-colic anastomosis with the anastomosis shown in Fig. 3. By joining the most distal point of the jejunum to the cæcum, both blind pouches were eliminated and all the remaining small and large bowel was exposed to the intestinal contents. During this procedure it was noted that the cæcum

TABLE I.—CASE C.V., LABORATORY DATA, DECEMBER 1956

Hæmoglobin value	12.2 g.%
Serum:	
Ca	4.3 mg.%
P	7.1 mg.%
Alk. phosphatase	9.5 Shinowara units %
K	2.9 mEq./l.
protein	6.2 g.%
non-protein nitrogen	35.0 mg.%

*From the Departments of Medicine and Surgery, Dalhousie University, and the Victoria General Hospital. Presented at the Annual Meeting of the Royal College of Physicians and Surgeons of Canada, Vancouver, B.C., January 23, 1959.

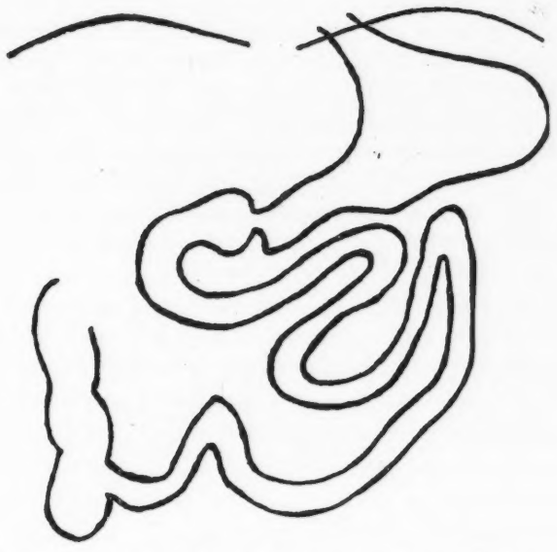

Fig. 3.—Diagram showing alteration of jejuno-colic anastomosis made in January 1957.

contained a greyish white fluid with a very sour odour. Unfortunately no specimen was taken for culture.

During the postoperative period the patient sustained a very gradual but marked improvement. Fig. 4 shows the very satisfactory weight gain which occurred, and his weight has been maintained subsequently at near normal levels. His appetite can only be satisfied by an excessively large food intake and at present he passes an average of two large foul stools per day. He has recently returned to lighter forms of manual labour. The patient received a gluten-free diet and intramuscular cortisone therapy for three weeks before the alteration of his anastomosis and for four months afterwards. There was some evidence that withdrawal of gluten resulted in symptomatic improvement, and during the early postoperative period the deliberate exhibition of gluten was associated with an exacerbation of diarrhœa. The

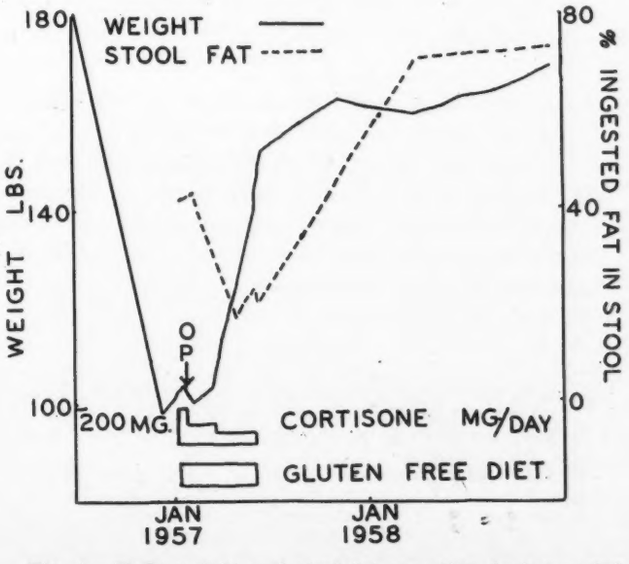

Fig. 4.—Body weight and stool fat excretion during period under observation.

stool fat analyses illustrated were made on three to four day pools which were collected after the patient had been on a 100 g. fat intake for three days. The lowest fat levels in stools were obtained in May and June 1957. It may be significant that the patient had received sulfisoxazole orally for six weeks before these analyses in addition to cortisone and a gluten-free diet. Since June 1957, the patient has, with minor exceptions, been without medication or dietary restriction. The striking increase in fat loss in the stools during this period is noteworthy. The oral glucose tolerance curve has also become completely flattened, whereas in June and November 1957 the peak blood sugar concentrations after glucose loading were about 40 mg. % above the fasting levels.

Fig. 5 shows the effect on stool fat excretion of adding gluten to a diet which had previously been gluten-free, at one month and again four

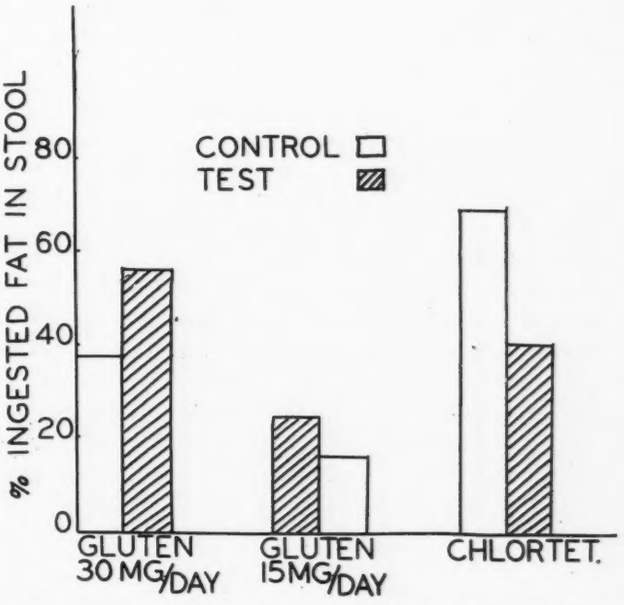

Fig. 5.—Effect of chlortetracycline and gluten on stool fat excretion.

months after alteration of the anastomosis. This diagram also shows the effect of oral chlortetracycline on fat excretion in the stools. The antibiotic was administered for a period of one week, at a time when there was no dietary restriction of gluten. The last-mentioned data suggested that alteration of the intestinal flora affected stool fat excretion. The addition or subtraction of cortisone therapy did not cause an immediate change in fat losses in the stools.

In November 1957 and again in April 1958, vitamin B_{12} absorption was markedly impaired as indicated by studies with cobalt-labelled vitamin B_{12} using the Schilling technique. Neither intrinsic factor nor chlortetracycline improved the patient's vitamin B_{12} absorption. It has been reported that this antibiotic improves B_{12} absorption in the blind loop syndrome, but not in primary steatorrhœa.[1]

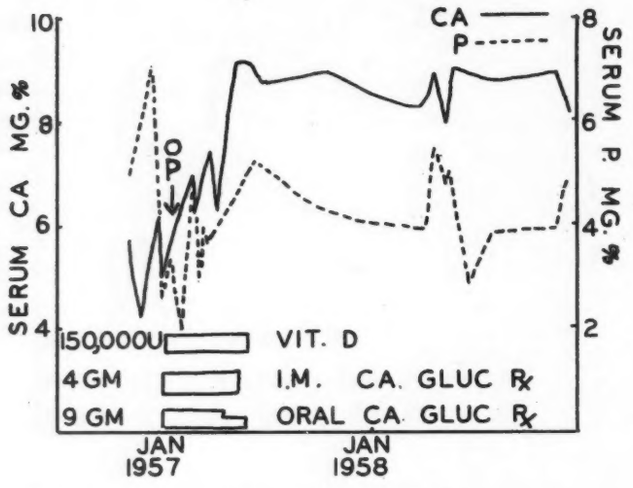

Fig. 6.—Serum calcium and phosphorus concentration during period under observation.

The patient has recently developed a macrocytic anæmia associated with megaloblastic changes in the bone marrow and these have responded to vitamin B_{12} therapy.

Fig. 6 shows the striking improvement in the serum calcium level after alteration of the anastomosis, and this was associated with disappearance of tetany and convulsions. Slight hypocalcæmia with a mean serum phosphate level of 4.5 mg. per 100 ml. have continued up to the present time. In December 1958, renal phosphate clearance was reduced to 2.25 ml. per minute (with normal creatinine clearance), findings which indicated the presence of hypoparathyroidism. This would not be expected in the hypocalcæmia of osteomalacia with secondary hyperparathyroidism.[2] The phosphaturic response to parathyroid hormone infusion was also impaired, but this was difficult to interpret because of the expected lowering from previous exposure to parathyroid hormone.

It seemed unlikely that osteomalacia was responsible for the slight hypocalcæmia which continued until the most recent examination, for the following additional reasons. The alkaline phosphatase level continued to be normal, and bone mineralization as determined radiologically was still satisfactory in December 1958. Appreciable calcium absorption occurred despite marked steatorrhœa as indicated by recent stool calcium losses of 73 mg. per day while the patient received a 200 mg. calcium intake. Urine calcium excretion was consistently low.

The lack of serum calcium response to parathyroid hormone before the alteration of the anastomosis may indicate that inactivation of parathyroid hormone was occurring or that the preparation used lacked potency. Hormonal inactivation has been demonstrated in a typical case of hypoparathyroidism by Harell-Steinberg.[3] Bensley and Cameron have reported subnormal phosphaturic responses to parathyroid hormone in steatorrhœa.[4] However, several mechanisms might be suggested to explain their findings.

We have not encountered published reports of malabsorption with hypocalcæmia in which the serum phosphorus level was elevated. We have under observation at the Victoria General Hospital three siblings with marked hypocalcæmia, evidence of malabsorption and hyperphosphatæmia. It is possible that malabsorption has given rise to the other abnormalities in these siblings, in view of the findings just reported

Steatorrhœa and hypocalcæmia are often associated with osteomalacia. Impaired calcium absorption has undoubtedly been present in those cases with high serum alkaline phosphatase and radiologically demonstrable bone disease. However, the recent report of Morgan and co-workers[5] of normal serum antirachitic activity in idiopathic steatorrhœa with hypocalcæmia indicated that these patients were not deficient in vitamin D. Furthermore, in those cases of malabsorption and hypocalcæmia with normal serum phosphate and phosphatase values, the possibility of hypoparathyroidism may require consideration as an alternative to first-degree osteomalacia. This suggestion is supported by Krane's report of hypoparathyroidism after thyroid surgery in which the hypocalcæmia was not accompanied by an elevated serum phosphate concentration.[6]

SUMMARY

Observations are presented on a patient with severe malabsorption syndrome after resection of all the small intestine except for the duodenum and 2½ to 3 feet of jejunum.

Severe hypocalcæmia resulted from hypoparathyroidism.

Alteration of a jejuno-colic anastomosis so as to eliminate two blind pouches and expose all remaining small and large bowel to the intestinal contents resulted in disappearance of undernutrition and convulsions, improvement as regards diarrhœa and hypocalcæmia, and the ability to return to light manual labour.

Impairment of absorption of vitamin B_{12} and glucose as well as steatorrhœa has persisted.

The present severe degree of steatorrhœa is for the most part not due to inadequacy of absorptive surface, because fat losses were only slightly abnormal in stools while the patient was on a gluten-free diet, cortisone, and oral sulfisoxazole.

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RÉSUMÉ

Un malade chez qui on avait réséqué tout le grêle sauf le duodenum et environ un mètre du jéjunum devint victime d'un syndrome de carences multiples. L'hypoparathyroïdie donna lieu à de l'hypocalcémie grave. Une modification de l'anastomose jéjunocolique élimina deux culs-de-sac et permit au chyme d'entrer en contact avec tout ce qui restait de la muqueuse. Les résultats furent encourageants. On observa la disparition de la dénutrition et des convulsions, ainsi qu'une diminution de la diarrhée et de l'hypocalcémie. L'amélioration de son état général permit au malade de retourner à un travail manuel léger. L'absorption de B_{12} et de glucose demeura inchangée. La stéatorrhée a persisté. Cette steatorrhée ne dépend pas du manque de surface d'absorption puisque la quantité de graisse dans les selles devint presque normale lorsque le malade fut mis à un régime sans gluten et reçut de la cortisone et du sulfisoxazole.

A SURVEY OF DUODENAL ULCER*
(724 Cases)

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THIS SURVEY of duodenal ulcer patients treated at the Winnipeg Clinic was undertaken to study our experience with this disease, especially in relation to such characteristics as the nature, frequency and severity of symptoms, the incidence of ulcer complications, the response to medical treatment, and the need for ulcer surgery. Since many of our patients proved to have duodenal ulcer failed to describe the usual "typical ulcer distress", a detailed study of symptomatology in this series was undertaken. It seemed of interest as well to see whether our medical treatment apparently altered the eventual course of this disease. The series has been divided into three groups of cases, the author's, those of other internists, and those of general surgeons, in order to allow a comparison of the results of treatment and the incidence of surgery under different doctors. Since the decision to advise operation in a case of duodenal ulcer is determined not only by the severity of the disease, but also by the attitude to surgery of both the doctor and the patient, an effort is made to analyze the relative importance of these factors in our patients subjected to operation.

MATERIAL AND METHODS

This report is based on a study of the records of 724 consecutive cases of duodenal ulcer seen at the Winnipeg Clinic in the three-year period 1952-1954. Cases were included in the survey if positive radiological or pathological evidence of duodenal ulcer was available. The radiological criteria consisted in the demonstration of the actual duodenal ulcer niche or the persistent duodenal deformity produced by it (see Table I). Since such clinical features of duodenal ulcer as typical pain, the incidence of complications, and the need for duodenal ulcer surgery were comparable in the group of 272 cases with persistent duodenal ulcer deformity but no crater on x-ray examination,

TABLE I.—THE DIAGNOSIS OF DUODENAL ULCER
(724 CASES)

Radiological criteria	
(Examination at Winnipeg Clinic)	
(a) Duodenal ulcer deformity with definite niche	336 cases
(b) Duodenal ulcer deformity with suggestive niche	54 "
(c) Duodenal ulcer deformity with no ulcer niche	272 "
(d) Duodenal ulcer niche (no other deformity)	31 "
(Examination elsewhere)	
"Duodenal ulcer"	5 "
	698 cases
Pathological criteria	
(No x-ray examination at clinic)	
(a) Emergency laparotomy for perforated duodenal ulcer	8 cases
(b) Elective remedial surgery for duodenal ulcer	15 "
(c) Unexpected finding at gastrectomy for gastric ulcer	2 "
(d) Diagnosis at necropsy	1 case
	26 cases
Total	724 cases

and the group of 336 cases with both deformity and crater, all were accepted as having duodenal ulcer disease.[1] Of the remaining cases, five were included on the basis of an acceptable x-ray examination done elsewhere, and in 25 the diagnosis was confirmed at laparotomy and in one case at necropsy.

For this survey the duration of the patient's dyspepsia was used to estimate the duration of his ulcer disease before our diagnosis, even though this might not always have coincided with the onset of peptic ulceration. This estimate, shown in Table II, totals more than 5000 ulcer patient years.

TABLE II.—DURATION OF DYSPEPSIA BEFORE DIAGNOSIS OF DUODENAL ULCER AT THE WINNIPEG CLINIC
(5365 PATIENT YEARS)

Less than 1 month	54 cases
1 month to 1 year	62 "
1 to 5 years	215 "
5 to 10 years	169 "
10 to 20 years	128 "
More than 20 years	65 "
Insufficient information	31 "
Total	724 cases

The follow-up period represents the time from our diagnosis until the patient's last visit before this survey, or until he underwent surgical treatment for his duodenal ulcer (except simple closure of a

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TABLE III.—DUODENAL ULCER
PERIOD OF OBSERVATION AT THE WINNIPEG CLINIC
(1667 PATIENT YEARS)

Less than 1 month	35 cases
1 to 11 months	138 "
1 to 2 years	122 "
2 to 3 years	89 "
3 to 4 years	78 "
4 to 5 years	40 "
5 to 10 years	74 "
More than 10 years	16 "
Single visit (back to referring doctor, etc.)	132 "
Total	724 cases

perforation). This estimate totalled about 1700 ulcer patient years, as shown in Table III. As mentioned above, the patients were divided into three groups according to their doctor, i.e. 219 cases under the care of the author, 277 cases under nine other internists, and 228 cases under five general surgeons. This permitted interesting comparison in regard to recorded symptoms, types and results of treatment, and the incidence of operation.

CLINICAL FEATURES OF DUODENAL ULCER

Sex Ratio:

This series comprises 532 males and 192 females, an approximate overall male/female ratio of 3:1. The ratio varied appreciably according to the severity of ulcer disease; the male/female ratio in those with hæmorrhage was 4:1, in those undergoing an operation for ulcer 5.5:1 and in those with perforation 10:1. It is obvious that in this series duodenal ulcer was a more serious disease in the males than in the females.

Age of Onset:

In the majority of our patients dyspepsia began in the third, fourth and fifth decades. Though unusual in our experience, symptoms first appeared in two patients during the first decade and in one as late as the ninth decade (Table IV).

TABLE IV.—AGE IN DECADES AT ONSET OF DYSPEPSIA IN DUODENAL ULCER

1st decade	2 cases
2nd "	62 "
3rd "	203 "
4th "	198 "
5th "	145 "
6th "	71 "
7th "	34 "
8th "	8 "
9th "	1 case

Occupation:

Deductions regarding duodenal ulcer susceptibility in various occupations are usually misleading unless mass surveys of the general population are carried out. Nevertheless, an effort to study this aspect was made by dividing our patients into the following categories: Group 1, those employed in an executive, professional or supervisory capacity; Group 2, office workers; Group 3, labourers and tradesmen; Group 4, farmers; Group 5, unclassified. Among the males the largest group was the labourers and tradesmen, comprising 40%; the farmers comprised 16%, as did those in Group 1. This information suggests that there is no special susceptibility to this disease among the professional, executive or supervisory personnel in our series.

Symptoms:

In reviewing the case records, the following symptomatology was considered as "typical ulcer distress": (1) epigastric distress of a "gnawing", "burning" or "aching" character; (2) epigastric distress occurring one or more hours after eating and relieved by taking food or alkali; (3) upper abdominal distress following a chronic recurrent course with exacerbations and remissions. If only two of these three general features were present, it was considered as *suggestive ulcer distress.* Less definite types of abdominal distress described by the patients as "gas", "bloating" or "fullness", and usually poorly localized, were considered as "functional distress". This included retrosternal burning sensations, i.e. "heartburn". All functional gastro-intestinal symptoms were subdivided according to whether they seemed predominantly of the upper or lower gastro-intestinal tract. Other symptoms noted were *vomiting* – whether of a reflex or obstructive nature; *night pain*—or ulcer distress awakening the patient after one to several hours of sleep, and *back pain* or ulcer pain referred or radiating to the lower dorsal or upper lumbar regions.

TABLE V.—SYMPTOMS IN PATIENTS WITH DUODENAL ULCER
(724 CASES)

Typical ulcer pain	56%
Suggestive ulcer pain	20%
Night pain	35%
Vomiting	21%
Back pain	12%
Functional distress (upper digestive tract)	49%
Functional distress (colon)	27%

The incidence of these various symptoms in the entire series is indicated in Table V. It will be seen at once that typical ulcer distress was noted in only 56% of the series. Almost as commonly recorded as typical ulcer distress was functional distress of the upper digestive tract, suggesting that a considerable number of our patients with duodenal ulcer experience symptoms of upper gastro-intestinal tract hyperirritability. Irritability of the colon, often described by the patient as flatulence or constipation, and frequently associated with the habit of using cathartics, was noted in 27% of the series. Night pain, quite a reliable feature of peptic ulcer activity, was noted at some time in 35% of these patients. Vomiting

was noted in 21% of the series, and the ulcer distress was referred to the back in 12% of cases. Some patients had ulcer pain radiating to the back during acute episodes and were promptly relieved by medical therapy—suggesting that this distress may be due to factors other than penetration of the pancreas by the ulcer.

In an effort to determine whether obtaining a typical ulcer history might be in part the result of the method in eliciting the history, the incidence was compared in groups of patients under the care of the internists, the author and the surgeons. A history typical or suggestive of ulcer was obtained in 70% of 277 cases by the internists, in 80% of 219 cases by the author, and in 66% of 228 cases by the surgeons. Although there is a tendency for the author and other internists to record an ulcer history more frequently than the surgeons, *it is evident that we all failed to obtain the usual ulcer history in from 20-34% of our cases.*

The pattern of ulcer symptoms varied from daily ulcer distress for weeks at a time to a few hours of distress on one or two days a week intermittently over a period of months. Some patients had complete remissions for months or years; others seemed to have less severe distress but of a more chronic nature, with remissions lasting only a few weeks in a year. As mentioned above, many patients with duodenal ulcer never have the usually expected ulcer symptoms.

COMPLICATIONS OF ULCER

(a) *Hæmorrhage.*—Satisfactory evidence of moderate or severe upper gastro-intestinal bleeding was found in 19% of this series of 724 cases. *A history of no ulcer pain was almost as common as was ulcer distress immediately preceding the episode of hæmorrhage.* This emphasizes the difficulty in relying on the history to make a diagnosis of ulcer in patients with hæmatemesis or melæna. Of 138 cases with bleeding, although 44% eventually underwent operation, in only one case was this necessary as an emergency procedure to stop the bleeding. Fifteen patients had an operation within a few days of the severe hæmorrhage being brought under control. The majority of patients with hæmorrhage underwent operation at a time unrelated to their episodes of bleeding.

(b) *Perforation.*—The ulcer perforated freely into the peritoneal cavity in 8% of this series of patients. In 50 patients this complication occurred before and in nine patients after the diagnosis at the Winnipeg Clinic. Although the perforation was closed without mortality in all cases, any curative ulcer surgery was undertaken at a second operation. In one of the author's cases, an elderly senile alcoholic patient, death occurred a few hours after admission to hospital, before a definite diagnosis of perforated duodenal ulcer had been made. He had minimal if any signs of peritonitis.

(c) *Obstruction.*—Obstruction was an uncommon complication, representing about 4% of the total series. These patients all had narrowing of the duodenal channel sufficient to result in marked gastric retention. All but two were treated surgically.

MEDICAL TREATMENT

This series of cases was treated medically by a variety of doctors, and there was no way of determining precisely the measures actually carried out by each patient. It has been assumed possible, however, to divide the type of therapy generally into three categories. The *ideal program* was one in which the patient took adequate rest in bed either at home or in hospital, accompanied by a reasonable program for acid control by frequent administration of alkali, small bland feedings, and sedative and antispasmodic drugs when necessary, with gradual resumption of activity over a period of several weeks. *Only 12% of this series carried out such a program.* About 50% attempted to control symptoms by these measures but while continuing at work. About one-third of the patients adopted a *casual program*, occasionally taking alkali or food when necessary to relieve ulcer distress, but being unable or unwilling to modify their way of life because of their ulcer tendency.

In general, the attending doctor outlined a program of treatment considered suitable to the patient, with regard to both the duration and severity of his symptoms and his willingness or ability to carry it out. If ulcer symptoms did not respond to this program within one or two weeks, more stringent measures were usually advised, i.e. the patient was told to stop work or modify his activities in a significant way for a period of rest. It was apparent that what approached ideal management was carried out only in the more severe cases and that even these patients seldom persisted in rest or alkali administration after a few weeks. The addition of anticholinergic drugs to the ulcer program is discussed below.

Anticholinergic Drugs:

During the period of this survey a continuing supply of new anticholinergic drugs was available for clinical trial. An effort has been made to assess the value of the addition of these drugs to the standard management of these patients with duodenal ulcer. Although approximately one-third of the patients received a trial of one or more of these drugs, insufficient information was available in 51 patients, leaving 178 for study.

The anticholinergic drugs used included eight quaternary and one tertiary amine derivatives. The names and number of patients using each are listed in Table VI. This indicates that of the 65 patients using methantheline (Banthine), three were subsequently treated with propantheline

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TABLE VI.—NUMBER OF CASES RECEIVING PARTICULAR ANTICHOLINERGIC DRUGS

Name of drugs	*No. of cases*	*Methantheline (Banthine)*	*Propantheline (Pro-Banthine)*	*Oxyphenonium (Antrenyl)*	*Mepiperphenidol (Darstine)*	*(Centrine)*	*Methscopolamine (Pamine)*	*Penthienate (Monodral)*	*Tridihexethenyl iodide (Pathilon)*	*Diphemanil (Prantal)*
Banthine	65		3	6	1		2			9
Probanthine	14	3		1	1	1	2			
Antrenyl	26	6	1		4	1	3		3	
Darstine	34	14	1	4			6	1	1	2
Centrine	5	1	1	1			3			
Pamine	18	5	2	3	5			1		
Monodral	2	1			2		1			
Pathilon	4			3	1					
Prantal	10	3		2	2					

(Pro-Banthine), six with oxyphenonium (Antrenyl), one with mepiperphenidol (Darstine) and two with methscopolamine bromide (Pamine) and nine with diphemanil (Prantal). Similarly, the number of patients using each of the other drugs is listed, indicating that these patients also tried a variety of the other available agents at one time or another.

These drugs were always combined with the usual medical measures, and the following criteria were set up to indicate significant benefit: (1) more rapid relief of symptoms, preferably in cases previously unresponsive; (2) more rapid healing of craters, with freedom from complications; (3) absence of intolerance to the drugs; (4) a preference or desire by the patient to use the anticholinergic drugs in the treatment of subsequent attacks; (5) a reduced incidence of surgery in the group using these drugs.

TABLE VII.—RESULTS OF THE ADDITION OF ANTICHOLINERGIC DRUGS TO THE MEDICAL TREATMENT OF DUODENAL ULCER

Stopped by patient because of side effects	8%
No apparent benefit to ulcer symptoms	16%
Apparent, partial or complete relief	50%
Failure to respond in subsequent attack	19%
Relief of pain but crater persists	6%
Relief of pain only with anticholinergic	8%
Patient always sought anticholinergic for subsequent attacks	10%
Incidence of remedial surgery	23%

The recommended dose or higher was given for three weeks or longer on 101 occasions to 80 patients, and for two months or longer on 49 occasions to 43 patients, six of these patients remaining continuously on medication for more than a year. There was no particular selection of cases, provided they did not meet the criteria for immediate surgical therapy. An assessment of the clinical value of these drugs may be deducted from Table VII. Side effects led to discontinuing the medication immediately in six patients and eventually in eight patients (approximately 8%). There was no apparent relief of ulcer pain within a week in 28 cases (16%). Use of the drug was associated within a week with partial relief of ulcer pain in 36 cases, and complete relief of ulcer pain in 44 cases (50%). *Partial or complete relief of ulcer symptoms within one week in only half the patients on the anticholinergic drug in addition to other measures certainly seemed of little additional help in the management.* In addition, 33 patients (19%), who apparently responded well initially, failed to do so in a subsequent attack. In 10 patients ulcer symptoms disappeared, with persistence of the ulcer crater radiologically 3-4 weeks later. In 8% of cases, anticholinergic drugs, when added to the therapeutic regimen, seemed to provide relief of symptoms when all previous measures had failed. However, this relief was temporary in two of these cases, which subsequently came to operation in spite of continuing with adequate anticholinergic dosage. Only 19 patients (approximately 10%) requested or used these drugs in each subsequent attack of ulcer distress and only two patients expressed a preference for one particular drug over the other they used. The five severe cases on continuous medication had recurrence of ulcer symptoms within a year. This group of drugs did not seem to protect against eventual surgery, as 27 cases using them for three weeks or longer eventually came to operation (23%) as compared to an overall incidence of operation in 21%.

RESULTS OF MEDICAL TREATMENT

The course of the duodenal ulcer disease in this series of patients has been assessed from a study of the number and severity of attacks of ulcer dyspepsia and of the frequency of ulcer complications. The following criteria have been set up for comparison of the course before and after the institution of medical therapy at the Winnipeg Clinic. Any recurrence of the patient's usual dyspepsia has been considered as an ulcer recurrence and has been classed as *mild*, unless it incapacitated him to the extent that he required rest at home or in the hospital, thereby interrupting his ability to work. When the patient had to stop work or go to bed for his symptoms it was classed as *severe*. The duration of his attack is listed as acute if it is less than 30 days and chronic if it persists longer, even though short remissions occurred. The *frequency of attacks* was listed as single, recurrent, or as occurring less than once in two years.

It appeared that the frequency and severity of attacks as related by the patients before diagnosis and treatment at the Winnipeg Clinic were not significantly different in the number of patients who either had complete remissions exceeding two years or whose attacks were consistently milder when followed up over a number of years. Some

TABLE VIII.—EPISODES OF HÆMORRHAGE PER 100 PATIENT YEARS BEFORE AND AFTER MEDICAL TREATMENT

	Prior to Winnipeg Clinic	*Follow-up period*
Estimated ulcer patient years	5365	1667
Episodes of hæmorrhage	183	30
Episodes per 100 patient years	3.4	1.8

patients did improve; but there were others who continued to have recurrences as before, and a few became worse. This applied to each of the three groups of cases, so that there seemed no significant difference whether the medical therapy was supervised by the author, another internist or a general surgeon.

Perhaps the results of medical treatment can be better assessed by comparing the incidence of such ulcer complications as perforation and hæmorrhage, since these episodes are more dramatic and hence better recorded. In regard to hæmorrhage, the incidence of episodes before diagnosis at the Winnipeg Clinic has been compared to that in the follow-up period in Table VIII and indicates a significant decrease. This may be misleading, since the more severe cases with hæmorrhage have been removed from the follow-up group by undergoing operation when first seen. In regard to perforation, we obtained the information outlined in Table IX. Before diagnosis at the Winnipeg Clinic the approximate incidence of perforation was 1 per 100 patient years. After our initial diagnosis of duodenal ulcer, the incidence of 0.6 per 100 patient years is obtained, indicating that our medical treatment may have reduced the incidence of perforation, but once again the more severe cases have been removed from follow-up by undergoing operation.

The author feels that, although we are able to assist the patient in arresting his current ulcer attack by medical treatment, any benefit derived seems limited to this period. As a group these ulcer patients continued to have about the same number of recurrent attacks, and although there may have been some reduction in complications after the institution of medical treatment, it is more likely that this is merely a reflection of the removal of the more severe cases from the follow-up group.

SURGERY IN DUODENAL ULCER

In this review we are primarily concerned with the incidence and type of operation performed. This has been compared in the three groups of

TABLE IX.—INCIDENCE OF PERFORATION PER 100 PATIENT YEARS BEFORE AND AFTER MEDICAL TREATMENT

	Prior to medical treatment	*Follow-up period*
Estimated ulcer patient years	5365	1667
Episodes of free perforation	50	10
Episodes per 100 patient years	1.0	0.6

TABLE X.—INCIDENCE AND TYPE OF SURGERY FOR DUODENAL ULCER

Type of surgery	*Internists*	*Author*	*Surgeons*
	277 cases	219 cases	228 cases
Gastrectomy	23 "	27 "*	62 "†
Gastroenterostomy and vagotomy	8 "	14 "	11 "
Gastrectomy and vagotomy		1 case	
Gastroenterostomy alone	1 case	3 cases	
Closure perforation	1 "	1 case	8 "
Incidence of surgery (approximate)	11%	20%	33%

*Four cases associated with gastric ulcer.

†Five cases had undergone gastroenterostomy elsewhere and were found to have: jejunal ulcer—1 case, gastric ulcer—2 cases, hæmorrhage (site uncertain)—2 cases.

cases. Studies of the results of surgical therapy in these cases have been reported elsewhere and are continuing.[2, 4] The type and incidence of operation are indicated in Table X. When computing the incidence of remedial ulcer surgery, simple closure of a perforation is not included. The varying incidence of surgery is impressive—11%, 20% and 33% in the three groups of cases. Many of the patients seen by the surgeons had more severe ulcer disease, being referred particularly for consideration of operation, so one would expect a higher incidence of operation in their group. Perhaps the author and the other internists were too conservative, since during the period of this study eight patients were known to have sought medical advice and undergone operation elsewhere, only one of whom was considered a candidate for surgery when last seen at the Winnipeg Clinic.

TABLE XI.
INCIDENCE OF IMMEDIATE AND ULTIMATE SURGERY

	Internist	*Author*	*Surgeon*
	277 cases	219 cases	228 cases
Immediate (within 30 days)	7 "	10 "	43 "
Ultimate (after 30 days)	26 " (9%)	35 " (17%)	30 " (16%)

Further study of the varying incidence of operation in the three groups is revealed in Table XI. After elimination of the cases referred for immediate surgery or considered to require operation at the first visit to the Winnipeg Clinic, there is still an increased incidence of operation among those under the surgeons' and the author's care. This might support the popular view that the surgeon is orientated towards surgical treatment and as a rule advises this earlier than the internist. There

TABLE XII.—DUODENAL ULCER, SEVERITY OF DISEASE

Groups of cases	*Male*	*Hæmorrhage*	*Perforation*
Internists	64%	21%	4%
Author	77%	38%	8%
Surgeons	81%	33%	14%

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are, however, features suggesting less severe ulcer disease in the group of cases seen by our internists, as shown in Table XII. Their group includes fewer males in whom the disease is more severe, and fewer cases with the serious complications. Thus, the smaller incidence of operation in the group of cases treated by the internist may be due to milder disease.

It was considered possible that many of our patients were operated on because they failed to carry out medical treatment in a diligent and comprehensive manner. In this regard the incidence of operation was compared between two groups of patients, i.e. those who carried out the strict and the casual treatment programs. The fact that approximately 40% of the patients on a strict treatment program underwent operation compared with 4% of those on the casual program suggests that more important factors than the type of therapy were responsible. It is suggested that the disease was of greater severity in those patients submitted to a strict regimen, and that this was the important factor determining not only whether or not operation became necessary, but also the type of medical therapy they carried out.

MORBIDITY AND MORTALITY

Duodenal ulcer causes a good deal of discomfort, but for the majority of patients it is not a lethal disease. Life insurance statistics based on 18,400 cases with 15 years' follow-up suggest that the mortality in persons with uncomplicated duodenal ulcer and not requiring operation is 1.2% of normal and in the complicated or surgical cases 1.9% of normal.[5] In our group of 724 patients during this period of observation there were two deaths due to duodenal ulcer in the medically treated group, both associated with perforation (approximately 0.4%). As mentioned earlier, an elderly senile and slightly intoxicated patient died a few hours after admission to hospital from an unsuspected perforation. The other patient would have been advised to undergo elective ulcer surgery except for severe coronary heart disease. He died of a second myocardial infarction occurring three days after perforation of his ulcer. In the group of patients treated surgically at the Winnipeg Clinic, one died of cardiac arrest a few minutes after the successful completion of an emergency gastrectomy for hæmorrhage as described above. Another patient died 10 days after partial gastrectomy with pancreatitis and massive hæmorrhage. This represents a surgical mortality of 1.3% in 154 operated cases. This compares with 4.4% in the period 1931-1940.[6]

The morbidity is more difficult to assess, varying to such a degree from person to person. During the period of this study only 12% of the patients were known to have been admitted to hospital or put to bed at home for one week or longer for conservative treatment of their ulcer. These patients were equally divided among those treated by the internists, the author or the surgeons. This would suggest that in the majority of patients with duodenal ulcer, their disease is largely a periodic nuisance until such time as complications or severe symptoms ensue.

DISCUSSION

The symptomatology in patients with peptic ulcer varies greatly, and current texts on this subject emphasize that the classical concept of ulcer distress must be broadened to include many other dyspeptic symptoms.[7-11] This study tends to support the contention that many patients with active duodenal ulcer fail to describe typical ulcer distress with pain—food—relief sequence. Many so-called "functional symptoms" may be the only history one obtains from certain patients with proven active duodenal ulcer disease. This is similar to our experience in patients with gastric ulcer.[12]

Current medical treatment[13] of patients with uncomplicated duodenal ulcer has been basically unchanged during the past 50 years since measures to control gastric acidity were first instituted. That such empirical therapy does little to prevent subsequent attacks is not surprising. In this study, little alteration in the eventual course of the disease was seen which could be solely attributed to our medical treatment. Anticholinergic drugs seemed of no additional value when added to general medical measures; this tends to support the critical appraisal of these drugs by others.[14] The factors determining which cases get worse and which improve are poorly understood but might provide the clue to more adequate ulcer treatment in the future, i.e. the prevention of subsequent relapses.

Patients with duodenal ulcer are subjected to operation for such a variety of reasons that comparing the incidence of operation in different series of cases is difficult. In our series the incidence of surgery appeared superficially to vary according to the type of doctor in charge of the case, but further analysis indicated that severity of disease was the more important determining factor. This concept of more severe ulcer disease in certain patients is important because it indicates that some patients continue to do badly in spite of all medical measures. If one can recognize such individuals, earlier surgical treatment for them is preferable to repeated periods of bed rest at home or in hospital.

The 21% incidence of operation in this group of ulcer patients is relatively high because of the selection of severe cases, many coming or being referred to the Winnipeg Clinic specifically for surgery. It is difficult to compare series of cases from different centres unless factors pertaining to the severity of disease are known. This can only be determined by assessing such details as the frequency and severity of symptoms and the incidence and severity of complications.

CONCLUSIONS

The clinical aspects of 724 cases of duodenal ulcer seen at the Winnipeg Clinic were studied.

Typical ulcer distress was described by only 60% and suggestive ulcer distress by another 25% of the series.

Hyperirritability of the gastro-intestinal tract was a common complaint, involving the lower œsophagus and gastric region in 50% and the colon and rectum in 27% of cases.

The type of medical treatment varied considerably, depending on such factors as the personality of the patient and the severity of his disease.

Medical treatment seemed to relieve symptoms and promote ulcer healing, but failed to reduce the incidence of recurrent attacks significantly.

Anticholinergic drugs failed to provide additional benefit when added to the usual ulcer program.

Complications of duodenal ulcer were hæmorrhage in 19%, perforation in 7%, and obstruction in 4% of cases.

The overall incidence of operation for duodenal ulcer was 21%, there being a significant difference in the groups of patients under the care of the other internists, the author, and the surgeons. Possible reasons for this variation are discussed.

The occurrence of complications and the need for ulcer surgery seemed to be determined more by the severity of ulcer disease than by the doctor in charge of the case, or the type of treatment carried out by the patient.

I wish to express my appreciation to Dr. Harold Fletcher, now in the Department of Gastroenterology, Royal Victoria Hospital, Montreal, for his help in the original review of the case records, and to Dr. P. H. T. Thorlakson for suggestions in the preparation of this manuscript.

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RÉSUMÉ

L'auteur a étudié l'aspect clinique de 724 cas d'ulcère duodénal vus à la clinique de Winnipeg. Seulement 60% des malades accusaient une symptomatologie typique; parmi les autres, 25% présentaient des symptômes évoquant quelque peu la présence d'ulcus. L'irritabilité des voies gastro-intestinales fut mentionnée fréquemment; dans 50% des cas elle portait sur l'œsophage inférieur et la région gastrique et dans 27%, sur le côlon et le rectum. Le genre de traitement médical varia considérablement d'après des facteurs tels que la personnalité du malade et la gravité de sa lésion. Ce traitement médical sembla soulager les symptômes et favoriser la guérison de l'ulcère mais n'arriva pas à diminuer sensiblement la fréquence des récidives. Les anticholinergiques n'ajoutèrent pas à l'amélioration que procure le traitement habituel de l'ulcère. Les complications de l'ulcère duodénal se répartirent comme suit: hémorragie dans 19% des cas, perforation dans 7% et occlusion dans 4%. En général la fréquence du traitement chirurgical s'éleva à 21%; il y eut cependant une différence importante à cet égard entre les groupes de malades sous les soins de l'auteur, des autres internistes et des chirurgiens. Le développement de complications et le besoin de recours à la chirurgie semblent dépendre plus de la gravité de la maladie ulcéreuse que du médecin chargé de la conduite du traitement ou du genre de traitement adopté par le malade.

A RESPIRATORY UNIT*
THE TORONTO GENERAL HOSPITAL UNIT FOR THE TREATMENT OF SEVERE RESPIRATORY INSUFFICIENCY

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THIS REPORT describes a unit for the treatment of respiratory insufficiency using intermittent positive pressure artificial respiration. Similar units have been established in other large medical centres. Intermittent positive pressure respiration has made possible the successful treatment of many conditions which have previously been fatal or whose treatment had been difficult and distressing. The conditions which have been treated in such units include poliomyelitis,[1] polyneuritis,[2] myasthenia gravis, central disorders of respiration due to multiple sclerosis, injury to the cord, overdosage of drugs,[3] head injury,[4] status epilepticus, CO_2 narcosis associated with chronic pulmonary disease, postoperative depression of respiration,[5] severe chest injuries,[6] tetanus,[7] and certain cases of acute respiratory disease.

In the Toronto General Hospital, patients with severe respiratory insufficiency were, until recently,

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treated without any special facilities on the ward to which they had been admitted. Tank respirators were used for patients with no spontaneous respiration and, occasionally, for patients breathing spontaneously but inadequately. The results obtained were often unsatisfactory. The rocking bed and cuirass respirator were useful only in those cases with relatively minor respiratory difficulties.

The disadvantages of the tank respirator were that ventilation of the patient, who had some spontaneous respiration, was often inadequate. The management of pharyngeal and pulmonary secretions was difficult, and medical examination, physiotherapy and nursing care were seriously hampered. Bed sores were common. The limitations of the tank respirator have become increasingly apparent with the need for artificial respiration in a wider range of conditions.

TABLE I.

A. MAY-OCTOBER 1958

Diagnosis	*Treated*	*Died*	*Recovered*
Polyneuritis	2	2	0
Postoperative respiratory failure	7	3	4
Stove-in chest	3	1	2
Barbiturate overdose	3	0	3
Myasthenia gravis	1	0	1
Multiple sclerosis	1	0	1
Total	17	6	11

B. OCTOBER 1958 - MARCH 1959

Diagnosis	*Treated*	*Died*	*Recovered*
Poliomyelitis	1	0	1
Postoperative respiratory failure	3	0	3
Stove-in chest	5	1	4
Barbiturate overdose	5	0	5
Myasthenia gravis	1	0	1
Emphysema and CO_2 narcosis	4	0	4
Tetanus	1	1	0
Status epilepticus	1	0	1
Total	21	2	19

A. Shows the cases treated in the 5 months prior to the opening of the respiratory unit;
B. Shows the cases treated in the first 5 months of operation of the unit.

In the spring of 1958, a group of staff physicians were appointed to make recommendations to improve this situation. Their recommendations were as follows:

1. A special unit should be established to which cases of respiratory insufficiency might be referred.

2. This unit should be permanently staffed by a specially trained group of graduate nurses.

3. Four physicians (a neurologist, a chest physician, an anæsthetist and an ear, nose and throat surgeon) should be appointed to take clinical charge of the unit. A thoracic surgeon should be available for consultation.

4. Intermittent positive pressure respiration (I.P.P.R.) should be used to ventilate most of these patients.

The principles of I.P.P.R. are those used in anæsthesia. The patient's lungs are mechanically inflated through a tracheostomy by air or oxygen. The patient's trachea is separated from the nasopharynx by an inflatable cuff round the tracheostomy tube.[8, 9] Expiration is passive. In the treatment of those who are expected to recover within 24 hours and, particularly, for the transport of patients to hospital for definitive treatment in the unit a cuffed orotracheal tube is used. Bronchial secretions are controlled by chest physiotherapy[10] and by suction through the tracheostomy.

The advantages of I.P.P.R. are its versatility and the easy access to the patient which it permits. These assets make the technique applicable to any type of case, including those with some spontaneous respiration. They permit easy and thorough clinical examination and physiotherapy and much more satisfactory nursing, and have altered the management of many conditions, notably of the patient with a severe chest injury. The main disadvantages of I.P.P.R. are the necessity for tracheostomy and the possibility of tracheal ulceration due to the use of a cuffed tube within the trachea.

The difficulties in the management of I.P.P.R., apart from the running of the machine and the establishment and maintenance of correct ventilation,[11] lie in the control of the airway, in the management of the tracheostomy and of the cuffed tube, and in the provision of adequate humidification of the inspired air.[12, 13] The successful use of I.P.P.R. depends upon constant attention to these details and upon the prompt recognition and correction of any deviation from normal. In achieving this, the advantages of a specialized unit have become apparent.

RESULTS

In the 10 months since the recommendations of the committee were made 38 patients have been treated, an average of one new patient every 10 days in a teaching hospital of 1200 beds. In practice the admissions to the unit have not been evenly distributed and short periods of relative inactivity alternated with periods of considerable activity.

Continuous artificial respiration was needed for periods of 12 hours to 4 weeks, and those patients who had more prolonged artificial respiration required a further period of weaning from the respirator before adequate spontaneous respiration was re-established.

The first of the committee's recommendations to be implemented was the appointment of the medi-

TABLE II.—SUMMARY OF THE MAIN FEATURES OF THE CASES TREATED IN THE FIRST FIVE MONTHS OF OPERATION OF THE UNIT

Diagnosis		*Age and sex*	*Time on respirator*	*Outcome*	*Remarks*
Tetanus		Male 69	17 days	Died	Incubation period? Evolution of symptoms—1 day. Severe kyphoscoliosis, arteriosclerotic heart disease with auricular fibrillation, cardiac failure and severe peripheral arteriosclerosis. Felty's syndrome. Died of staphylococcal septicæmia on 24th day.
Poliomyelitis		Male 31	7 days	Survived	Paralysis of bulbar and respiratory muscles, severe paresis of trunk muscles, quadriparesis. Residual paralyses—aphagia, weak flexion of neck and left hip. Speech good. Gastrostomy.
Postoperative respiratory failure	1	Female 35	12 hours	Survived	Reversible damage to medulla oblongata following removal of foramen magnum meningioma.
	2	Male 57	4 weeks	Survived	Severe diffuse bilateral bronchiectasis. Developed respiratory insufficiency following cholecystostomy.
	3	Male 21	4 weeks	Survived	Admitted one week after repair of A-V communis type of septal defect, with pump oxygenation. Extensive bilateral staphylococcal pneumonia and right pneumothorax, arterial O_2 47%, pH 7.2. Auricular flutter. Pulmonary abscess, left pneumothorax.
Stove-in chest	1	Male 32	1 week	Survived	Steering wheel injury. Six fractured ribs, fractured clavicle, all on one side. Major cause of respiratory insufficiency was thought to be sputum retention.
	2	Male 54	1 week	Survived	Riding accident, chest crushed under falling horse. Left—fractured clavicle, eight fractured ribs; right—acromioclavicular dislocation and four fractured ribs. Hæmatopneumothoraces. Gross surgical emphysema from vertex to waist.
	3	Male 84	4 weeks	Survived	Crushed against wall by truck. Floating sternum, 8 fractured ribs on right, 5 on left. Arteriosclerotic heart disease with auricular fibrillation. Chronic emphysema.
	4	Male 32	24 hours	Died	Attempted suicide. Run over by subway train. Multiple injuries, 4 fractured ribs left, fractured pelvis, ruptured viscera. Increasing respiratory distress for 3 days culminating in cardiac arrest. Resuscitated and then referred to respiratory unit in decerebrate rigidity.
	5	Male 72	3 weeks	Survived	Car accident. Fractured base of skull, acute subdural hæmatoma, multiple fractured ribs bilaterally, and fractured clavicle. Myocardial contusion, cardiac failure, auricular fibrillation.
Barbiturate poisoning	1	Male 64	7 days	Survived	Ingested phenobarbitone grains 60 and unknown quantity of other anticonvulsants. Recovery of consciousness in 10 days. *E. coli* septicæmia.
	2	Male 57	2 days	Survived	Ingested promazine (Sparine) 1.25 g. and secobarbital (Seconal) grains 22. Aspirated vomit. Recovered consciousness on 3rd day.
	3	Male 18	24 hours	Survived	Schizophrenic. Ingested unknown quantity of phenobarbitone. Full recovery of consciousness on 4th day.
	4	Female 34	18 hours	Survived	Ingested amobarbital (Na Amytal) grains 25 (approx.). Oro-tracheal tube. Full recovery of consciousness in 36 hours.
	5	Male 52	10 hours	Survived	Alcoholic on disulfiram (Antabuse). Ingested unknown quantity of whisky, beer, secobarbital and meprobamate. Full recovery of consciousness 15 hours. Oro-tracheal tube.
Emphysema and CO_2 narcosis	1	Male 71	20 days	Survived	Moribund after administration of morphine gr. 1/4. Severe right heart failure. CO_2 combining power 96 vol.%. Slow improvement.
	2	Male 53	12 days	Survived	Respiratory infection; restless, disorientated. CO_2 combining power 86 vol.%. Rapid improvement.
	3	Male 59	18 days	Survived	Respiratory infection, unconscious, cyanosed, appeared moribund. Arterial CO_2 tension 113 mm. Hg. Slow improvement.
	4	Male 44	14 days	Survived	Respiratory infection. Restless, hallucinated, tremor. Slow improvement.

TABLE II.—SUMMARY OF THE MAIN FEATURES OF THE CASES TREATED IN THE FIRST FIVE MONTHS OF OPERATION OF THE UNIT

Diagnosis	*Age and sex*	*Time on respirator*	*Outcome*	*Remarks*
Myasthenia gravis....	Female 29	14 hours	Survived	Post-thymectomy. Universal paralysis due to anticholinesterase poisoning. Oro-tracheal tube.
Status epilepticus....	Female 18	2 days	Survived	Status epilepticus on first post-partum day. Gross depression of ventilation due to seizures and sedatives without control of seizures. Controlled with relaxants.

cal team, in an advisory capacity, and the purchase of two constant pressure I.P.P.R. machines. In the next five months, 17 cases were treated on the wards to which they had been admitted. No specially trained nurses and no other equipment for ventilation or for the monitoring of ventilation were available. These deficiencies hampered the efficiency of the team. The outcome of these cases is shown in Table IA. Six deaths occurred, of which three (two polyneuritides and one postoperative case) were thought to be due to errors in the management of artificial respiration. The other three deaths were due respectively to renal failure, infection and multiple injuries.

In October 1958, four beds, in temporary accommodation, were made available to the team. Nurses were appointed to staff this unit, and their training and that of the physiotherapists was started. Methods of monitoring ventilation were set up. Various types of I.P.P.R. machine were acquired. In the subsequent five months (Table IB), 21 patients were treated in the unit with two deaths, neither attributable to errors in the management of artificial respiration. One, a patient with tetanus, died of staphylococcal septicæmia on his 24th hospital day. His tetanus, which had required continuous treatment with relaxants and I.P.P.R. for 17 days, had ceased to be a serious problem seven days before his death. The other patient was referred to the unit on his 5th hospital day in a decerebrate state, after an episode of cardiac arrest for five minutes; death was attributed to medullary damage. The other 19 patients all left hospital and returned to their usual occupations, save three; one was transferred to a mental hospital for the treatment of schizophrenia, one is suffering from post-traumatic seizures and one is undergoing neurological investigation. Two cases of tracheal ulceration occurred, in the patient with tetanus and in one of the patients with stove-in chest who made a complete recovery from his tracheal ulcer and his chest injury. The details of these 21 cases are shown in Table II.

Since the establishment of the unit, there has been a marked reduction in the number of occasions when medical aid has been urgently required for a patient in the unit. This is due to the ability of the trained nurse to detect and correct minor disturbances (e.g. in ventilator function, airway patency, etc.) before they cause major and urgent trouble. Careful suction and prompt recognition of the need for suction, together with skilled chest physiotherapy, have made lobar collapse a most infrequent occurrence. Three serious infections have been acquired by patients while in the unit: a staphylococcal septicæmia which was fatal, an *E. coli* pyelonephritis and septicæmia in a patient with barbiturate poisoning and an *H. influenzæ* pneumonia in a patient with emphysema. No bed sores have occurred.

Four patients had cardiac failure, two due to arteriosclerotic heart disease and auricular fibrillation and two due to cor pulmonale. In all cases the heart failure responded to the usual measures.

In conclusion, many conditions may cause inadequate respiration and, hence, hypoxia and carbon dioxide retention. This cannot be relieved by the administration of oxygen and is the usual immediate cause of death. In many of these cases the primary condition is potentially reversible. Even in patients apparently dying, the institution of adequate ventilation by the methods described usually leads to striking improvement and eventual return to a normal life. Accordingly we have had to revise our criteria of "hopelessness" in such cases.

SUMMARY

A unit has been set up at the Toronto General Hospital for the treatment of severe respiratory insufficiency.

The unit is staffed by a team of four physicians and a permanent group of specially trained nurses.

Ventilation is maintained by the technique of intermittent positive pressure respiration (I.P.P.R.).

The results of treatment in the unit are compared with the results obtained before the unit was set up.

The establishment of a special unit has resulted in more efficient treatment and more satisfactory results in the survival and return to their usual occupations of these patients.

Our thanks are due to Dr. W. B. Oille, the Chairman of the Sub-Committee on Respiratory Insufficiency, for his advice and encouragement.

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RÉSUMÉ

Le traitement de certaines formes de défaillance respiratoire grave comme on en voit dans les blessures graves de la cage thoracique et de la poitrine, la poliomyélite, la polynévrite, la myasthénie, la dépression des centres respiratoires, le tétanos et autres atteintes semblables, présente certaines difficultés particulières. En vue de les surmonter l'hôpital général de Toronto a formé une équipe composée de quatre médecins et d'un groupe permanent de gardes-malades spécialement formées à cette fin. Le traitement de ces malades consiste à insuffler mécaniquement leurs poumons par de l'air ou de l'oxygène humides par voie de trachéotomie. Cette technique est connue sous le nom de *respiration par pression positive intermittente*. La phase expiratoire est passive. Les risques d'ulcération de la trachée que comporte cette méthode sont compensés par l'accès facile du malade à tous ceux qui en ont soin pour fins d'examen, de physiothérapie et de nursing. La comparaison des résultats obtenus avant la formation de cette équipe et depuis, a montré qu'une telle unité procure des soins plus efficaces et des résultats plus satisfaisants dans la survie et le retour au travail des malades ainsi traités.

EXPERIENCE WITH GLIPASOL (R.P. 2259)*—AN ANTIDIABETIC SULFONAMIDE DRUG†

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THE EFFECTS of an antidiabetic sulfonamide drug, R.P. 2259 or Glipasol®*, were studied in 31 patients with maturity-onset diabetes mellitus. This drug is one of the sulfonamide drugs upon which the investigations of Loubatières and his colleagues were performed in France during and after the Second World War.[1] It differs from carbutamide and tolbutamide (Fig. 1) in that it possesses a

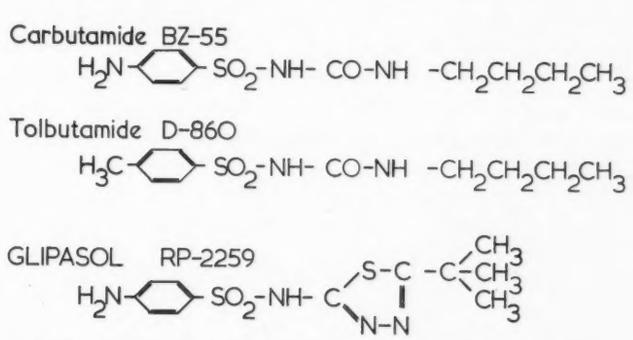

Fig. 1.—Structural formulæ of three hypoglycæmic sulfonamides.

thiodiazole rather than a urea nucleus and has a tertiary rather than a normal butyl end prosthetic group. It also resembles carbutamide and differs from tolbutamide in having an amine group substituted on the benzene ring. Though many of the thiodiazole drugs were less effective hypoglycæmic agents than were the sulfonylureas, Loubatières[2] found the tertiary-butyl derivative (R.P. 2259 or Glipasol) to be as effective and as well tolerated in diabetic patients as were carbutamide and tolbutamide. This drug, Glipasol, has been marketed in France for the past year by the Rhône-Poulenc Company, and neither in general clinical use nor in the initial clinical trials have serious toxic reactions been reported.[3]

CLINICAL MATERIAL AND METHODS

Thirty-one adult male patients with maturity-onset diabetes, untreated or receiving insulin, were chosen at random from those attending the out-patient diabetic clinic and from inpatients at Shaughnessy Hospital. Pertinent data on these patients are shown in Table I. One patient was 46 years old, two were between 50 and 59 years, fifteen between 60 and 69, twelve between 70 and 79, and one patient was 80 years old. Thus, all but four patients were between 60 and 70 years of age. Using 10 lb. each side of average weight as the limits of "normal"*, it was found that seven patients were underweight, eight overweight, and sixteen "normal" or of average weight. Ten of the patients had been known to have diabetes for less than 5 years, seven from 5 to 9 years, nine from 10 to 14 years, and the remaining five patients from 15 to 19 years. Fifteen patients had taken insulin for less than 5 years, four for 5 to 9 years, nine for 10 to 14 years, and the other three from 15 to 19 years. Insulin dosage required for optimal control of the diabetic state ranged from 15 to 90 units daily; seven patients took less than 30 units, eleven took 30 to 49 units, seven took 50 to 69 units, and six required 70 units or more. In assessing the degree of control of the diabetic state achieved both with insulin and with Glipasol, the following criteria were used: excellent control, two-thirds of fasting blood sugar determinations 120 mg.% or lower; good control, two-thirds of fasting blood sugar levels 140 mg.% or lower; fair, two-thirds of levels 180 mg.% or lower; and poor control, these requirements not met. Previous control with insulin had been excellent or good in 15 of the 31 cases, only fair in nine cases, and poor in four cases. Three patients, newly diagnosed (Nos. 4, 26 and 27), were not assessed in this regard. Only six patients had previously shown evidence of ketosis (Nos. 3, 5, 6, 11, 21 and 24) and one of these was in diabetic coma at the time of diagnosis.

*R.P. 2259, (Glipasol, Poulenc), 2-sulfamido-p-aminobenzene-5-terbutyl-1-thio-3, 4-diazole, was supplied by Poulenc Limited, Montreal, Canada, in pink, scored, 500-mg. tablets.

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*Tables of the Life Extension Institute of New York City.4

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TABLE I.—THE DIABETIC STATE AND ITS CONTROL BEFORE AND DURING THE ADMINISTRATION OF GLIPASOL IN THIRTY-ONE MALE PATIENTS WITH MATURITY-ONSET DIABETES MELLITUS.

Patient No.	Age years	Weight (lb.) and height (inches)	Known duration of		Previous state of control	Previous ketosis (known)	Complications related or possibly related to diabetes	Final control with insulin			Prescr. diet (Cal/d)	Control during Glipasol administration				
			D.M. years	Insulin therapy (years)				Daily insulin dosage (units)	Successive fasting blood sugar levels (mg.%)	Time interval (days)		Glipasol dosage (g./d)	Fasting blood sugar range and average (mg.%)	No. tests	Total days of administr.	Control achieved
1*	62	154 69	13	8	Fair	0	Retinopathy A.S.H.D.** (infarction)	30	142,105,138	4	1800	1.0 2.0 3.0 4.0	158-170 (164) 148-162 (155) 155-164 (160) 135-161 (149)	2 3 2 4	2 7 10 16	Fair
2	67	121 66	8	4	Fair	0		15	134,124	7	2550	1.0	97-158 (124)	4	82	Good
3	75	137 64	10	10	Fair	Mild	A.S.H.D.**	35	119,128, 92	4	1600	1.0 1.5 2.0	119-139 (132) 106-127 (114) 94-100 (97)	5 5 3	13 46 77	Excellent
4*	71	140 68	4/12			0		20	178,118,146	3	2100	1.0 2.0 2.5 2.5-3.0	157-200 (179) 134-155 (145) 117-132 (125) 95-134 (108)	3 3 2 6	3 9 14 77	Excellent
5	73	146 65	6	3	Excellent	Mild	A.S.H.D.**	35	110,118,131	3	2350	1.0 1.5	120-124 (122) 96-120 (109)	2 13	6 76	Excellent
6*	68	113 63	4/12	4/12	Poor	Coma		60	114, 96,120	4	2200	3.0 4.5†	264 160-276 (210)	1 5	4 14	Poor
7*	73	143 66	2	2	Good	0		20	123,162,126	3	1350	1.0 1.5	110-132 (121) 120	7 1	13 19	Excellent
8	80	160 70½	6	6	Good	0	Retinopathy A.S.H.D.** (infarction)	15	124,108,138	3	2000	1.0-1.5 1.5	126-134 (131) 123-138 (129)	4 4	20 77	Good
9	66	204 72	6	6	Good	0	Retinopathy Periph. neuritis	30	100,131,111	5	1800	2.0 2.5-3.0	123-144 (133) 119-139 (129)	2 3	20 67	Good
10	64	180 67	18	18	Poor	0	Retinopathy	60	300,314	2	1800	3.0 3.5-4.0	106-260 (175) 184-222 (200)	5 4	13 74	Poor
11	61	135 68	17	17	Fair	Mild	Retinopathy A.S.H.D.**	50	114,128	3	2000	2.0 2.5-4.5	181-195 (188) ††	2	6 15	Poor
12	78	151 66½	10	10	Fair	0	A.S.H.D.**	50	111,102	3	1800	1.0-1.5 1.5-2.0	146-158 (150) 135	4 1	34 46	Fair
13*	62	148 66	8	4	Excellent	0	A.S.H.D.**	30	119, 98, 93	5	2000 2200	1.0 2.0-2.5 3.0-4.5	101-138 (115) 103-134 (116) 100-150 (125)	2 10 11	4 27 73	Good
14	79	120 67½	1½	1½	Good	0	Retinopathy A.S.H.D.**	40	137,133	8		1.5	127-148 (136)	3	42	Good
15*	78	122 67	2		Fair	0	A.S.H.D.** Periph. neuritis	50	78, 65, 94	3	1300	1.5 2.0	82-117 (103) 103-124 (111)	5 7	19 62	Excellent
16	75	170 69	5	4	Good	0	Cataract A.S.H.D.**	50	124,108,107	7	1600	1.0 1.5	105-128 (115) 115	4 1	48 91	Excellent
17	62	178 69	14	14	Fair	0	Retinopathy A.S.H.D.** Periph. neuritis	90	139,108,140	8	2000	2.0 2.5-3.0 3.0	174 109 141-196 (159)	1 1 3	4 16 21	Fair
18	54	187 66½	14	3	Good	0		80	112, 93,108	5	1000	2.0 2.5-3.0	92-144 (118) 92-138 (122)	2 5	6 58	Good
19	65	133 69	6	6	Excellent	0	Retinopathy Periph. neuritis	15	116, 88,102	6	1800	1.0 1.5	96-125 (108)	5	38 57	Excellent
20*	69	154 66½	2	2	Excellent	0	A.S.**	45	105, 93	2	1900	1.0	104-125 (114)	5	35	Excellent
21	77	152 64	13	13	Fair	Mild	Retinopathy A.S.H.D.** Periph. neuritis	70	140,118,110	4	1800	2.0 3.0 4.0	181-193 (187) 180 190-244 (217)	2 1 2	6 12 16	Poor
22	75	133 69	2	2	Excellent	0	A.S.** Periph. neuritis	30	98, 97	4	1800	1.0 1.5	110-130 (119) 99-101 (100)	5 2	31 36	Excellent
23	60	140 68	13	13	Good	0	Cataracts	42	112,109,111	6	1600	1.5 2.0	180 142-147 (145)	1 2	13 34	Fair
24	76	155 68	16	12	Poor	Mod.	Cataract A.S.H.D.** Infected ulcers	40	135,148,112	4	2000	1.5 2.5-3.0†	405-561 (483) 164	2 1	6 8	Poor
25	63	182 68	18	10	Excellent	0	A.S.H.D.** (infarction)	25	78, 80,105	5	2000	1.5 2.0	127-134 (131) 125	3 1	7 35	Good
26*	73	169 65	1/12	1/12		0		70	110, 97,112	4	1850	1.0 1.5-2.0	155 114-135 (124)	1 4	3 20	Good
27*	69	181 74	1/12	1/12		0		80	116, 96, 84	5	2400	2.0 2.5-3.0	185-192 (188) 102-159 (131)	3 4	3 16	Good
28*	46	164 68	12	12	Poor	0		60	105, 52,108	3	2500	2.0 3.0-4.0†	270-292 (281) 152-300 (243)	2 6	2 10	Poor
29	69	156 69	1	1	Excellent	0	Periph. neuritis	45	114, 94,125	6	2300	1.5 2.0	125-142 (134) 100-145 (122)	2 2	8 23	Good
30	58	156 68	13	13	Fair	0		15	154,158	2	2400	1.0	128-145 (135)	3	12	Good
31	64	178 72	17	17	Excellent	0	A.S.H.D.** (infarction) Periph. neuritis	74	97,112,109	5	1750	2.0	166-300 (222)	3	21	Poor

*Hospitalized during control with Glipasol.
**A.S.H.D.—arteriosclerotic heart disease; A.S.—arteriosclerotic peripheral vascular disease.

††Glipasol discontinued because of symptoms.
†Insulin given in addition to Glipasol.

Each patient was brought into careful, optimal control of the diabetic state by adjustment of the insulin dosage with frequent (daily when possible) fasting blood sugar determinations and three urinalyses a day for sugar with Clinitest (Ames). The diet prescribed was fixed, appropriate to the individual patient, of the exchange type, and was maintained throughout the period of study. Data regarding insulin and Glipasol therapy and diet prescribed for each case are shown in Table I.

In order to follow the degree of control of the diabetes, and to determine any possible toxic drug reactions, the following laboratory procedures were carried out on each patient during the control period and at frequent intervals during the administration of Glipasol: determination of fasting blood sugar level (Folin-Wu, modified); urinalysis, routine and microscopic; hæmoglobin estimation, total and differential white blood cell count, and determination of erythrocyte sedimentation rate (modified Westergren method); determinations of blood nonprotein nitrogen,[5] serum cholesterol,[6] bromsulphalein retention (45 minutes except in a few early tests in which 30-minute determinations were performed),[7] thymol turbidity,[8] cephalin-cholesterol flocculation,[9] total serum proteins, albumin and globulin.[10] Later in the study total and direct-reacting serum bilirubin levels[11] and serum alkaline phosphatase activity[12] were also determined at frequent intervals. Needle biopsy specimens of the liver were obtained in five patients (Nos. 5, 7, 17, 22 and 25) by the transthoracic approach.

In most cases 1.0 gram a day of Glipasol was used initially and the dosage increased from this level as indicated by fasting blood sugar determinations. In some patients who required high doses of insulin, 1.5 or 2.0 grams and in one case 3.0 grams daily was used from the start of Glipasol therapy.

RESULTS

Table I shows the data relative to the degree of control achieved with Glipasol therapy in the 31 patients studied. Nine patients demonstrated "excellent" control, eleven showed "good" control, four showed only "fair" control, and seven showed "poor" or no response. Those with an "excellent" or "good" response to therapy with Glipasol will be described separately from the remaining cases, in which the diabetes was not considered controlled by the drug.

Patients with Diabetes Controlled by Glipasol

Blood sugar levels in 20 of the 31 patients (65%) were well controlled. Seven of these (Nos. 4, 7, 13, 15, 20, 26 and 27) received Glipasol while in hospital and the remainder were treated on an outpatient basis.

Age.—Two patients were 54 and 58 years old, eight were between 60 and 69, nine were between 70 and 79, and one (No. 8) was 80 years old.

Known duration of diabetes.—In nine of the patients, diabetes mellitus had been diagnosed within five years. Four (Nos. 4, 26, 27 and 29) were known to have had diabetes for only a year or less, and one of these, patient No. 4, who received insulin for only a few days before starting Glipasol therapy, subsequently responded excellently to the latter drug. Two patients in whom the diagnosis and treatment with insulin was of one month's duration (Nos. 26 and 27) showed a good response to the drug, though one of them (No. 26) subsequently "escaped" from control at the time of the development of evidence of hepatic dysfunction. Seven patients had been known to be diabetic for from 5 to 9 years, three from 10 to 14 years, and only one (No. 25) for more than 15 years.

Duration of insulin therapy.—Fourteen patients had been receiving insulin for less than 5 years, three from 5 to 9 years, and three from 10 to 14 years. None of the patients whose diabetes was controlled with Glipasol had been on insulin for 15 years or longer. All but two of the patients with excellent control had been taking insulin for less than 5 years. These two (Nos. 3 and 19) had been on insulin therapy for 10 and 6 years respectively.

Insulin dosage.—The usual dose of insulin previously required for diabetic control ranged from 15 to 80 units. Seven had taken less than 30 units, eight from 30 to 49 units, two from 50 to 69 units, and three had required 70 or more units. All of those patients with an excellent response to Glipasol had taken 50 units of insulin daily, or less. In two patients (Nos. 26 and 27) who required 70 and 80 units respectively, diabetes had been recognized for only one month, and both responded well to Glipasol for 20 and 16 days respectively, after which the drug was discontinued. One other patient (No. 18), a known diabetic for 15 years, who was well controlled by 80 units of protamine zinc insulin daily, had taken insulin for only three years. He showed a good response to therapy with Glipasol.

Previous control.—Seven of the 20 patients who responded to the drug had previously shown excellent control of the diabetic state with insulin, six had had good control, and four had shown only fair control. None of the patients whose blood sugar levels were controlled by Glipasol had had poor control with insulin therapy.

Previous known ketosis.—Previous evidence of ketosis, at the time of the original diagnosis of diabetes, was present in only two of the patients (Nos. 3 and 5) controlled by Glipasol; both gave an excellent response to the drug.

Weight.—Half of the controlled patients were of average weight and two of these had previously been overweight and had lost weight at the time of and since the diagnosis of diabetes (Nos. 20 and 29). Five patients were underweight (Nos. 2, 14,

15, 19 and 22) and of these only one (No. 22) had always been thin. The other four had lost 20 to 40 lb. since the onset of symptoms of diabetes. None of these patients had been known to have ketosis. Five patients were overweight (Nos. 9, 16, 18, 25 and 26); all of these had previously weighed even more, but had lost weight at the time of diagnosis or, by restriction of caloric intake, since diagnosis. Three of the underweight patients showed excellent response to Glipasol, as did one of those overweight.

Associated conditions.—Seven of the patients controlled by Glipasol (Nos. 2, 4, 7, 18, 26, 27 and 30) exhibited no evidence of diabetic complications. The known duration of diabetes in these patients was under five years except in patients Nos. 18 and 30, in which it was 12 and 13 years respectively. The remaining 13 patients who responded well had evidence of arteriosclerotic heart disease in ten cases, with myocardial infarction in two patients (Nos. 8 and 25), diabetic retinopathy in four cases, cataracts in one case, and peripheral neuritis in five cases. Three patients had had frequent infections, and in two (Nos. 13 and 22) the diagnosis of pulmonary tuberculosis had been made in the past.

Patients with Diabetes Not Controlled by Glipasol

Eleven patients (35%) showed only fair or poor response to Glipasol therapy. Three (Nos. 1, 6 and 28) were given Glipasol while in hospital, the remainder in the outpatient department.

Age.—One patient (No. 28) was 46 years old, seven were between 60 and 69 years, and the remaining three were between 70 and 79 years of age.

Known duration of diabetes.—Only one of the patients whose diabetes was not controlled by this drug had had diabetes for less than 10 years. The diagnosis in this man (No. 6) had been made four months earlier, when he had been admitted in diabetic coma. The other ten patients had been known to have diabetes for at least 10 years, six for from 10 to 14 years, and four during 15 to 19 years.

Duration of insulin therapy.—Patient No. 6 was the only one who had taken insulin for less than 5 years. One other had taken insulin for 8 years, six others for from 10 to 14 years, and the remaining three for from 15 to 19 years.

Insulin dosage.—Three patients required 30 to 49 units of insulin daily, five required 50 to 69 units, and three (Nos. 17, 21 and 31) 70 units or more. Each of these latter three who required high doses of insulin had been taking insulin for more than 10 years (14, 13 and 17 years respectively).

Previous control.—Nine of the 11 patients whose diabetes was not controlled by Glipasol had also not had adequate previous control with insulin. Only one patient (No. 31) had previously had excellent control, and one (No. 23) had had good control. All four who had previously had poor control (Nos. 6, 11, 24 and 28) also gave a poor response to Glipasol.

Weight.—Two patients (Nos. 6 and 11) were underweight when the present study was started and both had lost weight before the diagnosis of diabetes. Six patients were of average weight, and three (Nos. 10, 17 and 21) were obese.

Previous known ketosis.—Four patients, including the two underweight, had had evidence of ketosis at some time. One of these (No. 6) had had severe acidosis, and two others (Nos. 11 and 21) had had mild acetonuria at the time of diagnosis. The other (No. 24) developed acetonuria when therapy with Glipasol was commenced.

Associated conditions.— Only two of the patients (Nos. 6 and 28) did not show clinical evidence of diabetic complications. Of the remaining nine, five had diabetic retinopathy, two had cataracts, two had peripheral vascular disease, eight had arteriosclerosis with myocardial infarction in two cases, and three had peripheral neuritis.

The history of one patient, described in detail elsewhere,[13] is worthy of note, in that he died during the attempt to control his fasting blood sugar levels with Glipasol.

CASE 24.—G.B., aged 76. Diabetes mellitus was first recognized in 1942, when he was admitted to hospital for furunculosis. A low calorie diet was prescribed. Control of his diabetic state was poor until 1946 when insulin was first given. After this he had frequent mild and occasional severe insulin reactions. In 1949 he was receiving 1900 calories and 30 units protamine zinc insulin daily. At this time he first complained of shortness of breath on exertion, angina, and intermittent claudication with persistent numbness of the feet. The first of several admissions for infected ulcers of the lower leg was in 1956. Diabetes was out of control at each admission but was subsequently controlled with 35 to 40 units isophane (NPH) insulin and 1600 to 2000 calories.

In the outpatient department on September 16, 1958, a fasting blood sugar level was 135 mg.%. Other conditions present included arteriosclerotic heart disease with angina pectoris and congestive heart failure, peripheral arteriosclerosis, and peripheral neuritis. There was a right cataract and arteriosclerotic retinopathy in the left eye. Blood pressure was 185/85 mm. Hg and pulse 84 and regular. He continued to receive 2000 calories and 40 units NPH insulin daily. Fasting blood sugar levels on September 17 and 19 were 148 and 112 mg.% respectively. Insulin was discontinued on September 19 and he was given 1.5 g. Glipasol daily. On September 23, the fasting blood sugar level was 405 mg.%. He was admitted to hospital on September 25, because of malaise, anorexia, polydipsia and polyuria. A fasting blood sugar level was 561 mg.%. There was no evidence of infection. Glipasol was increased to 3.0 g. daily and he was given 100 units regular insulin at noon. He continued to show + 4 glycosuria and at noon and 4:00 p.m. had + 2 and + 3 acetonuria respectively. A blood sugar level at 3:00 p.m. was 666 mg.% and he was given 200

units regular insulin at 4:30 p.m. He received a total of 2.5 g. Glipasol on this day. Fasting blood sugar on September 26 measured 164 mg.%. He felt considerably better and his appetite returned. By 3:00 p.m. the blood sugar level had risen to 540 mg.% and he was given 150 units of regular insulin at 5:00 p.m. He received a total of 3.0 g. Glipasol on this day. At 1:30 a.m. on September 27, he was apparently well but within the next 30 minutes he suddenly became unconscious and died.

Autopsy performed 8½ hours after death revealed severe coronary atherosclerosis and acute myocardial infarction. The pancreas weighed 57.8 g.; 1.8 g. was removed for histological examination. The remainder was rapidly frozen, packed in dry ice, and shipped by air express to the C. H. Best Institute, Toronto, where insulin extraction and assay was carried out by Dr. G. A. Wrenshall. The extractable insulin was found to be "too low to measure".[13]

Toxic effects due to Glipasol were noted during the present clinical trial. Six of 31 patients developed jaundice, and in five of these a liver biopsy specimen was obtained. The histological findings were those of hepatitis. All specimens showed varying degrees of diffuse parenchymal degeneration, marked nuclear variation, and scattered areas of focal necrosis. There was prominent portal and periportal inflammation in four cases, and the exudate contained many eosinophils in three cases. The clinical and laboratory findings and the histological features of the liver biopsies of these patients are to be reported.[14] Eleven other patients showed laboratory evidence of hepatic dysfunction reflected in abnormal retention of bromsulphalein. In three patients there was also increased urinary urobilinogen, and in one there was increased serum alkaline phosphatase activity. All 17 patients with hepatic dysfunction recovered uneventfully except that two (Nos. 7 and 19) had continued abnormal retention of bromsulphalein six months after the cessation of Glipasol therapy.

The occurrence of hepatic dysfunction was found to be unrelated to age, known duration of diabetes or of insulin therapy, insulin dosage required for previous control of the diabetic state, or the duration, daily dose or total dose of Glipasol administered. In 14 of the 17 patients manifesting hepatic dysfunction, the blood sugar levels had been well controlled by Glipasol. In only three patients was a fair or poor response noted.

Three patients with previous evidence of ketosis, whose condition was poorly controlled by Glipasol (Nos. 6, 11 and 21) developed symptoms of malaise, anorexia, slight nausea, and weakness or faintness shortly after being given Glipasol therapy. One other who was poorly controlled (No. 28) developed drowsiness and confusion when his blood sugar levels rose. Three patients who had good diabetic control with Glipasol (Nos. 8, 18 and 19) complained of troublesome belching and flatus associated with a feeling of abdominal fullness. Two of these (Nos. 8 and 19) in addition had slight anorexia.

Seven patients of the 31 given Glipasol had eosinophil counts of 10% or higher during the course of therapy. Four of these were patients who developed jaundice (Nos. 7, 17, 22 and 26) and the liver biopsy specimens of three of these showed many eosinophils in the portal and periportal inflammatory exudate. The other (No. 26) had had 14% eosinophils before receiving Glipasol; he was found to have pinworm infestation. Two other patients with evidence of hepatic dysfunction but no jaundice (Nos. 18 and 27) developed eosinophil counts of 10 and 11% respectively. One other patient, No. 13, developed no evidence of hepatic toxicity, but had up to 19% eosinophils during therapy with Glipasol.

Four patients who received Glipasol had total white blood cell counts of 4000 per c.mm. or less during the course of therapy. One of these, patient No. 28, unsuccessfully controlled with Glipasol, whose white blood cell count after six days of therapy with this drug was 2950 per c.mm., was also receiving diphenylhydantoin sodium (Dilantin Sodium, Parke-Davis). However, his white cell count five days before starting Glipasol had been 6000 per c.mm. Two other patients (Nos. 2 and 18) had total white cell counts of 4000 and 3800 respectively while receiving Glipasol therapy. In each, previous white cell counts had been 5200. The white cell count of patient No. 10 was initially 8200 and fell to 3400 after 74 days of Glipasol therapy. The differential count showed 48% neutrophils, 2% staff cells, 35% lymphocytes, 5% monocytes, 1% basophils and 9% eosinophils.

Repeated urinalyses in each patient revealed no abnormalities that could be attributed to Glipasol therapy.

DISCUSSION

Twenty of the 31 patients (65%) with maturity-onset diabetes who received Glipasol responded favourably to the drug, with either excellent or good control of fasting blood sugar levels. This compares favourably with the results obtained with carbutamide and tolbutamide.[15-21]

Although the mechanism of action of the oral sulfonamide drugs is not completely understood, it appears that to be effective they require a certain supply of endogenous insulin.[13, 22] Patients with maturity-onset diabetes have widely variable amounts of extractable pancreatic insulin, the average amount being more than 40% of the non-diabetic control levels.[23] However, an average of 31% of patients with maturity-onset diabetes have an extractable pancreatic reserve of one-tenth or less as much insulin as have nondiabetic human controls.[13] The diabetes of most of these persons is comparable to the insulin-deficient diabetes of patients with growth-onset diabetes and would not be expected to respond to the oral sulfonamide drugs now in use. In the present study, one patient (No. 24), known to be diabetic for 16 years, re-

TABLE II.—CORRELATION OF VARIOUS FACTORS WITH THE ADEQUACY OF CONTROL OF BLOOD SUGAR LEVELS WITH GLIPASOL IN 31 PATIENTS WITH MATURITY-ONSET DIABETES.

	Number of patients	*Number with adequate control (excellent or good)*	*Number with inadequate control (poor or fair)*
Total	31	20	11
Age: 40 - 49	1		1
50 - 59	2	2	
60 - 69	15	8	7
70 - 79	12	9	3
80	1	1	
Weight:			
Underweight	7	5	2
Average weight	16	10	6
Overweight	8	5	3
Known ketosis	6	2	4
No known ketosis	25	18	7
Known duration of diabetes:			
0 - 4 years	10	9	1
5 - 9	7	7	
10 - 14	9	3	6
15 - 19	5	1	4
Duration of insulin therapy:			
0 - 4 years	15	14	1
5 - 9	4	3	1
10 - 14	9	3	6
15 - 19	3		3
Previous insulin dosage:			
10 - 29 units	7	7	
30 - 49	11	8	3
50 - 69	7	2	5
70 and over	6	3	3
Previous control:	(28)*	(17)	(11)
Excellent	8	7	1
Good	7	6	1
Fair	9	4	5
Poor	4		4

*Three patients in whom diabetes was recently diagnosed are not assessed in this regard.

quired 40 units of NPH insulin for control and did not respond to Glipasol therapy. The extractable insulin of his pancreas was found to be "too low to measure".

As shown in Table II, there is a considerable difference in the known duration of diabetes between those cases controlled and those not controlled with Glipasol. Four patients achieved good control by this drug though they were known to have had diabetes for at least 10 years. Diabetes in ten of the 11 patients whose disease was not controlled by Glipasol had been recognized for 10 years or longer. Control of the diabetic state was either poor or fair in four of the five patients whose known duration of diabetes was between 15 and 19 years. Many patients in whom diabetes has been recognized for over 15 years respond to therapy with tolbutamide.[15] In this regard, according to Wrenshall and Best,[22] "a progressively decreasing frequency of effectiveness of the oral therapy in maturity-onset subjects of both sexes with increasing years of survival after diabetes diagnosis is matched by a slow decrease in the average amount of insulin extractable from the pancreas, also averaged for both sexes, but mainly assignable to the male subjects."

As shown in Table II, there was also a difference in duration of previous insulin therapy between those cases controlled and those not controlled with Glipasol. Nine of the 11 patients whose diabetes was uncontrolled by Glipasol had taken insulin for 10 years or more, whereas only three of the 20 patients whose diabetes was controlled by the drug had been on insulin therapy for 10 years or more.

All of the patients in the present series were over 45 years of age. In this small group of patients, the response to the drug was similar in each age class, as shown in Table II. Of 127 patients treated with tolbutamide by Sugar,[17] diabetic control was equally successful in those between 40 and 59 years of age and in those between 60 and 80 years.

The diabetic state of one patient who had had diabetic coma was not controlled by Glipasol. Five other patients had a history of mild ketosis; in three of these diabetes was not controlled with Glipasol. Similar experience with tolbutamide has been reported by Dolger.[18] In four patients, including the one with a past history of diabetic coma, control of diabetes had been difficult with insulin and they had had frequent hyperglycæmia and hypoglycæmic reactions. They did not respond to therapy with Glipasol. Table II shows the relationship between the previous degree of control of the diabetic state with insulin and the subsequent effectiveness of Glipasol. Of the 15 patients who had had excellent or good control with insulin, 13 had similar degrees of control with Glipasol. Of the 13 patients who had shown fair or poor control with insulin, nine responded similarly to treatment with Glipasol.

According to Dolger,[18] successful treatment with tolbutamide is infrequent in those requiring more than 50 units of insulin daily, although striking success can occasionally be obtained in those requiring larger doses. Sugar[17] found that 10 of 15 patients who required 60-85 units of insulin daily were treated successfully with tolbutamide. In the present study, there were three patients whose diabetes was well controlled by Glipasol though they previously required 70 units or more of insulin, and two who had required 50-69 units. Of the 11 with poor or fair control with Glipasol, three had previously taken 70 units or more of insulin daily, and five had taken 50-69 units.

Several investigators have reported the occurrence of toxic effects due to carbutamide or tolbutamide in animal studies.[24-26] The occurrence of skin rash, pruritus and other mild reactions has been attributed to therapy with tolbutamide.[17, 27] A variety of toxic effects due to carbutamide have been reported.[28] In 1957, Field and Federman[29] described a case of sudden death in a patient

receiving carbutamide, in whom autopsy revealed some changes similar to those previously described in patients with lesions attributable to sulfonamide medication.[30] Camerini-Dávalos, Root and Marble[31] reported the occurrence of jaundice in four patients receiving carbutamide, and subsequently performed liver function tests in a group of control patients and in those receiving carbutamide.[19] They found that a large number of the patients taking carbutamide developed abnormal retention of bromsulphalein and increased serum alkaline phosphatase activity, and a smaller number had abnormal thymol turbidity and cephalin cholesterol flocculation tests.

The use of Glipasol in the present clinical study was abandoned because of the large number of patients who developed evidence of hepatic dysfunction. Six patients developed jaundice and in addition eleven others had increased retention of bromsulphalein. Liver biopsy, performed in five of the patients with elevated serum bilirubin levels, showed varying degrees of diffuse parenchymal degeneration, focal areas of necrosis, and portal and periportal inflammation. One patient who had been jaundiced (No. 7) and one who had not (No. 19) showed a persistently increased retention of bromsulphalein six months after therapy with Glipasol was discontinued.

SUMMARY AND CONCLUSIONS

Thirty-one adult male patients with maturity-onset diabetes mellitus were given an antidiabetic sulfonamide drug, R.P. 2259 (Glipasol). These patients ranged from 46 to 80 years of age, had been known to have diabetes for from a few weeks to 18 years, and had been controlled with from 15 to 90 units of insulin daily; all except four had been easily controlled previously with insulin.

Glipasol satisfactorily controlled the blood sugar levels in 20 (65%) of the patients.

The effectiveness of Glipasol was unrelated to age (all patients were over 45 years). It was less effective in patients who had had known diabetes for 10 years or more, in those who had received insulin therapy for 10 years or more, in those who required more than 50 units of insulin daily, and in those whose diabetes had previously been difficult to control with insulin.

Seventeen or 54% of the patients developed laboratory evidence of hepatic dysfunction while receiving Glipasol. Liver biopsy in five patients with jaundice showed hepatitis characterized by parenchymal involvement and portal and periportal inflammation. This drug is therefore considered to be too toxic for clinical use.

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RÉSUMÉ

R.P. 2259, un sulfamide hypoglycémiant connu dans le commerce sous le nom de Glipasol (*marque déposée*), servit au traitement de 31 hommes adultes dont le diabète avait débuté durant l'âge mûr. L'âge de ces malades s'étendait de 46 à 80 ans. Leur état datait de quelques semaines à 18 ans et répondait à une dose quotidienne de 15 à 90 unités d'insuline, sauf pour quatre d'entre eux qui avaient présenté quelques difficultés de contrôle. Six malades faisaient de la cétose. Le Glipasol régularisa la glycémie de 20 malades ou 65% du groupe. Son efficacité n'avait pas de rapport avec l'âge puisque dans cette série tous les malades avaient plus de 40 ans. On remarqua un rendement inférieur chez les malades dont le diabète datait de 10 ans ou plus, chez ceux qui avaient reçu de l'insuline pendant 10 ans ou plus, chez ceux dont le besoin quotidien d'insuline dépassait 50 unités et chez ceux dont le diabète n'avait pas bien répondu à l'insuline. Dix-huit malades ou 58% du groupe montrèrent des signes d'insuffisance hépatique d'après les données du laboratoire, alors qu'ils recevaient du Glipasol. Des ponctions-biopsies du foie chez cinq malades atteints de jaunisse montrèrent une hépatite caractérisée par une atteinte parenchymateuse et une réaction inflammatoire autour des canalicules. Ce médicament semble donc trop toxique pour servir à l'usage clinique.

SPONTANEOUS PERFORATION OF THE COMMON BILE DUCT

Though rare, spontaneous perforation of the bile duct in infancy can be diagnosed and successfully treated. The present case, from Copenhagen, is the 11th reported, and the patient was a 4½-month-old girl.

The characteristics common to these cases were: mild onset, subacute course, recurrent jaundice, gross abdominal distension, ascites, and in many cases large bilateral inguinal hernias. The perforation of the common bile duct was not always found, but drainage of the region was often sufficient for complete recovery, and without operation recovery has not been reported. The etiology is obscure. There is no bile in the urine. Operative cholecystocholangiography is recommended.—*I. C. Gertz, A.M.A. Arch. Surg.*, 78: 7, 1959.

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Case Reports

CYSTICERCOSIS CEREBRI*

P. A. RECHNITZER, W. SUTHERLAND and C. G. DRAKE, *London, Ont.*

ALTHOUGH infection of the human brain with the larval form of the pork tapeworm (cysticerci of *Tænia solium*) is not uncommon in many parts of the world, it has been rare in the United States and Canada. In a recent review of the literature, White *et al.*[1] collected three published cases which had been operated on in the United States and added three of their own, in two of which craniotomy was performed. In Canada, Parkinson and Childe[2] reported a patient in whom they removed two cysts from the fourth ventricle. In retrospect, the diagnosis of cysticercosis cerebri seems likely. In 1956, Owen and Lenczner[3] reported two cases in immigrants living in Toronto.

Understanding of the pathogenesis of cysticercosis cerebri depends upon a knowledge of the life cycle of the parasite. Man is the definitive host for the adult tapeworm, which he acquires by eating undercooked pork containing the larval form. The larva then develops into the adult tapeworm in the intestine. The worm discharges its egg-bearing segments in the fæces. When the eggs are ingested by pigs, they develop into mobile larvæ in the intestine and are then able to penetrate the intestinal wall and reach the blood stream. They are transported to the muscles of the porcine host where they form cysticerci. If, however, man ingests the eggs, as may occur with fæcal contamination of food, the larval form will develop in the human intestine and is able to reach the blood stream and to be disseminated throughout the body. One of the most common sites for encystment is the brain, where the condition is called cysticercosis cerebri.

When the larvæ reach the human brain, three types of infection may result: (1) A solitary cyst may give rise to symptoms suggesting a cerebral neoplasm. (2) Widespread infection may result from multiple cysticerci scattered throughout the brain. (3) Hydrocephalus may be produced by a proliferative inflammatory reaction in the basilar meninges.

In the case described below, the cyst was situated at the caudal end of the fourth ventricle where it was producing symptoms of increased intracranial pressure, intermittent at first but later continuous. It seems likely that movement of the cyst was able to produce intermittent blockage of cerebrospinal fluid flow. Surgical removal of the cyst resulted in complete relief of symptoms.

*From the Department of Medicine, University of Western Ontario, and St. Joseph's Hospital, London, Ontario.

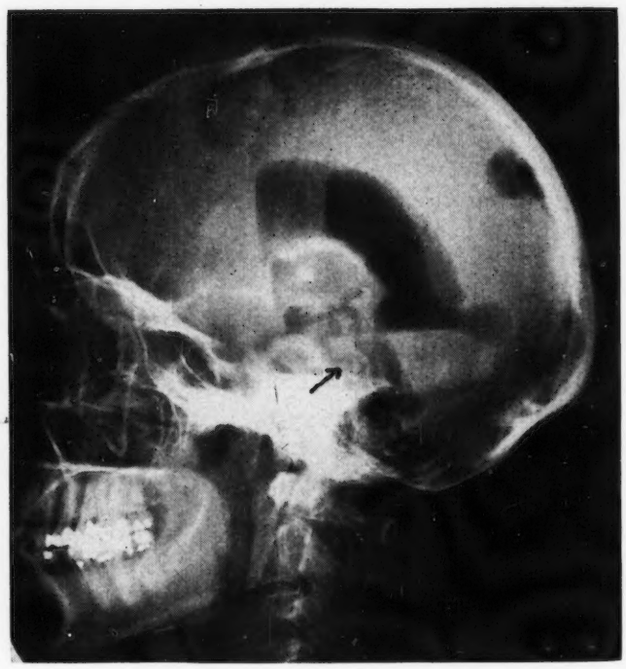

Fig. 1.—Ventriculogram, lateral view. Dilated lateral and third ventricles and aqueduct with posterior convexity deformity of the floor of the fourth ventricle adjacent to the aqueduct.

M.L., a 29-year-old housewife, was perfectly well until October 28, 1957, when she experienced sudden vertigo and vomiting. The vomiting subsided after ten minutes, and the patient felt much better. A similar episode occurred on the following day. In early November, an upper gastro-intestinal x-ray series and gall-bladder series were carried out in another hospital and were negative. During November and December, the patient had frequent attacks of vomiting, unaccompanied by nausea. There were intervals as long as a week between attacks. The patient was in hospital for three weeks and given intravenous fluids. While in hospital she developed bronchopneumonia, which responded to antibiotic therapy. During this period in hospital the patient was free of vomiting for approximately 12 days. She returned home for a week, but the vomiting recurred and the patient was readmitted to hospital and subsequently transferred to St. Joseph's Hospital, London.

The patient had been born in Poland and removed to a concentration camp in Russia in 1940. Subsequently, she lived in Africa for seven years and during that period she had malaria. In 1949, the patient emigrated to Canada, where she has lived since. She was married in 1956 and had a normal delivery in July 1957.

On examination, she was moderately dehydrated and had gross bilateral nystagmus on lateral gaze as well as upward gaze. She had bilateral papillœdema, more marked on the left side. An ataxia had not been observed before, but had suddenly become marked on the day of admission to hospital. Reflexes were normal and equal. Plantar stimulation evoked a plantar response. The remainder of the physical examination was normal. Urinalysis was negative, hæmoglobin value was 14.8 g. %, non-protein nitrogen was 20 mg. % and fasting blood sugar was 102 mg. %. Skull radiographs showed evidence of increased intracranial pressure manifested by demineralization of the dorsum sellæ. There was no abnormal calcification or localizing

signs of a space-occupying lesion. The ventriculogram showed moderate dilation of the ventricular system (Fig. 1), with a small mass occupying the caudal portion of the enlarged fourth ventricle. At craniotomy (C.D.), a smooth-walled yellow cyst about the size of a large grape with a one-inch tail was removed from the lower end of the fourth ventricle. Microscopic examination revealed this to be a cysticercosis cyst (Fig. 2).

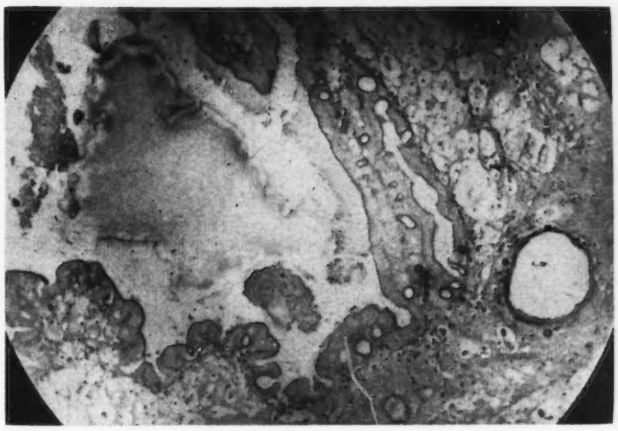

Fig. 2.—*Tænia solium* cyst—low power view.

On the eighth postoperative day the patient developed fever, right anterior chest pain and hæmoptysis. Radiography revealed consolidation involving the right upper lobe. A diagnosis of pulmonary infarction was made and the patient was given anticoagulant therapy with heparin and dicoumarol. The patient's subsequent postoperative recovery was uncomplicated and she was discharged on the 26th postoperative day. Examination of fæces for ova was negative, and radiographs of the extremities failed to reveal evidence of calcification in the muscles. The patient was last seen 15 months after the operation, feeling entirely well. Follow-up neurological examination was negative.

SUMMARY

A case of cysticercosis cerebri is described. The symptoms, due to obstructive hydrocephalus, were considered preoperatively to be due to a posterior fossa tumour. After removal of the cyst the patient improved, and except for delayed convalescence due to a pulmonary infarct, she made an uneventful recovery and is now symptom-free and normally active again.

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SIMULATION OF TETANUS BY TRIFLUOPERAZINE OVERDOSAGE*

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R.A., a mentally defective boy of 19, was transferred to the Ontario Hospital, Kingston, on January 27, 1959, from the Ontario Hospital, Orillia, where he had received chlorpromazine 75 mg. and phenobarbital grains 6 daily in divided doses for the previous six weeks. As his treatment sheet had been mislaid on arrival, and as his condition remained satisfactory, it was decided to discontinue medication and watch his behaviour before prescribing for him.

Two days later he became agitated and hyperactive, and trifluoperazine (Stelazine) was prescribed. The dose was increased daily, until on the fifth day he was ordered 25 mg. twice a day. His condition steadily improved for the next three days, and this prescription was not altered. On the morning of the eighth day, he was behaving quite normally, engaging in ward activities, but in the afternoon he was flushed and was found to have a temperature of 105° F. There were no other physical signs at that time, but soon afterwards he had a convulsion, and it was noticed that his back and neck were stiff. Trifluoperazine was discontinued. It was thought possible that he was developing meningitis, but the cerebrospinal fluid was normal. By the morning of the ninth day after commencement of trifluoperazine, his muscles were all very stiff, he was doubly incontinent and there were moist sounds throughout the chest. On the 10th day, he was extremely rigid and he had difficulty in swallowing. Trismus and opisthotonos were present, and every few minutes there was a tetanic contraction of his whole musculature, arching of the back and trismus being most marked.

At this point tetanus was considered as the diagnosis, and several healing abrasions were noted on the extremities. Whilst antitetanic serum was being obtained, it was found that the last order for trifluoperazine had been miscopied, and he had in fact been getting 100 mg. a day, altogether a total of 420 mg. in seven days. Trihexyphenidyl (Artane) 4 mg. was given, and the tetanic contractions ceased, although he was still rigid. Trihexyphenidyl was continued in 4-mg. doses three times a day.

On the 11th day the chest was clear, the temperature was 102° F., and there was still slight Parkinsonism. By the 13th day he had made a complete recovery, though his temperature was still 100° F., and this did not reach normal until the 16th day. During this illness he was given antibiotics, and chloral hydrate for sedation; trihexyphenidyl was discontinued on the 13th day.

DISCUSSION

Dyskinetic syndromes are well known in phenothiazine administration and they occur earlier and with greater severity in derivatives with a higher potency, such as trifluoperazine. Mandibular tics, difficulties in speech and swallowing due to hypertonicity, and hyperextensor spasms and seizures have been noted.[1]

*From the Ontario Hospital, Kingston.

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In the present case, one might have speculated upon the withdrawal of barbiturates as an accentuating factor, although the long delay of eight days would argue against this. Thus, if the cortex were left in a hyperexcitable state, there might be less inhibition from higher areas to counteract whatever the subcortical effect of trifluoperazine might be.

In the treatment of such a condition, paradoxically, both a cerebral stimulant (namely caffeine) and cerebral depressants (namely barbiturates) have been claimed to give good results. Anti-parkinsonian drugs seem to be the best available remedy, and we wish to stress the lability and reversibility of this rather frightening condition which may simulate tetanus. With increased use of high-potency phenothiazines, such syndromes may cause confusion and may result, as in this case, from the inadvertent prescription of a higher dosage than usual.

My thanks are due to Dr. C. H. McCuaig, medical superintendent of the Ontario Hospital, Kingston, and to Dr. R. Bruce Sloane for his advice in the preparation of this article.

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SHORT COMMUNICATION

ISOLATION OF A HÆMADSORPTION VIRUS FROM THE RECENT OUTBREAK OF RESPIRATORY ILLNESS IN ONTARIO*

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MEHROO R. COOPER, M.D.,
L. P. MORRISSEY and
J. LESIAK, *Toronto*

DURING the recent outbreak of influenza-like illness among school children as well as adults, a hæmadsorption virus was isolated. This non-influenza virus was recovered from 78 out of 175 specimens submitted from different parts of Ontario. Judging from the dates of receipt of specimens, the outbreak began about the middle of January 1959, reached its peak during March, and, gradually subsiding, ended about the end of April. In at least one community 30% of the population were affected by this illness. In addition to the usual influenza-like symptoms, a considerable number of patients had cervical adenitis. A detailed clinical picture of this illness will be reported separately.[1] The present brief communication deals with the methods of isolation, identification and some of the characteristics of this virus.

*From the Virus Diagnostic Unit, Central Laboratory, Ontario Department of Health, Toronto 4, Ontario.

ISOLATION OF VIRUS

Throat washings, collected in most cases within three days after onset of symptoms, were delivered to the laboratory in the frozen state. Each specimen was treated with 1000 units of penicillin and 1000 μg. of streptomycin per ml. and inoculated into monolayer monkey-kidney tissue cultures, HeLa cells and developing chick embryos.

Monkey-kidney tissue cultures were maintained in Medium HB597[2] at 37° C. No cytopathogenic changes were observed in the inoculated cultures even after 10 days of incubation, and the presence of the virus was demonstrable only by hæmadsorption technique[3] and by hæmagglutination with the fluid phase of tissue culture, using either guinea pig or human type O erythrocytes. Even continuous serial passage of the virus did not result in production of specific cytopathogenic changes. On initial isolation the maximum hæmadsorption was observed five days after inoculation. On subsequent passage hæmadsorption was detectable as early as 48 hours after inoculation, reaching its maximum by the end of 72 hours. Attempts at propagation of this virus in HeLa cell tissue cultures were unsuccessful both with the original specimens and with monkey-kidney passage virus. Even after four blind passages neither hæmadsorption nor hæmagglutination with HeLa tissue culture fluids was evident.

Embryonated eggs at various stages of development (7 to 11 days of incubation) were inoculated into amniotic sacs in triplicate series and each series incubated at different temperatures (34° C., 35° C. and 37° C.). In this manner only 13 isolations were made from 44 specimens found to be positive by tissue culture methods. Neither age of the embryos nor the different temperatures had any apparent effect on the results of attempts at isolation. Growth of the virus in eggs under the various conditions tried was rather poor. Hæmagglutination technique was used for the detection of the virus in amniotic fluid. Antiserum prepared for one of the chick embryo isolates neutralized and inhibited hæmadsorption of several tissue culture isolates that failed to grow in the chick embryo, thus indicating that isolates from both sources were antigenically the same.

SOME OF THE CHARACTERISTICS OF THE ISOLATED VIRUS

Sufficient evidence has been obtained to demonstrate that the isolated agent is a virus. This is shown by its ability to pass through a bacteria-tight filter (Fritted Disc, ultra-fine porosity) and its failure to grow on artificial media (tryptose broth, tryptose agar, blood agar, MacConkey's and brain broth) under various conditions. Further, no organisms were demonstrable in the stained smears of infected tissue culture fluids.

The virus, which henceforth will be referred to as 433 virus, grew quite readily in monkey-kidney tissue cultures. The usual infective titre ($TCID_{50}$) of the fluids was found to be 10^{-8}. The virus, while quite stable at 4° C., was inactivated at 58° C. in 30 min. without destruction of hæmagglutinating activity. The virus was also inactivated by 20% ether within 20 min. Both guinea pig and human type O erythrocytes were equally suited for

hæmadsorption and hæmagglutination reactions. The latter reaction took place equally well at 24° C. and 4° C. The virus was adsorbed by and readily eluted from erythrocytes. Heating at 58° C., however, altered it, so that while still adsorbable it could not be eluted.

RELATIONSHIP TO OTHER VIRUSES

To establish the relationship of 433 virus to other viruses, neutralization, hæmadsorption inhibition and hæmagglutination inhibition tests were performed. In hæmagglutination inhibition, either untreated infected tissue culture fluid or virus concentrated by adsorption on red blood cells and subsequent elution was used. All sera for this test were treated with potassium periodate.[4] Hæmadsorption and hæmagglutination were not inhibited and the virus was not neutralized by various influenza antisera, NDV, mumps, Copenhagen 222 or hæmadsorption Type II[5] high-titre antisera.*

Hæmadsorption Type I[5] antiserum, however, did inhibit four hæmagglutinating units of 433 virus in the dilution up to 1:160, but the same antiserum diluted 1:10 failed to inhibit hæmadsorption and failed to neutralize 433 virus. Hæmadsorption inhibition titre of this antiserum with homologous virus was 1:640.

When human type O erythrocytes after adsorption and elution with 433 virus were treated with 1% trypsin for one hour, they lost their ability to agglutinate in the presence of 433 virus and hæmadsorption Type I and Type II viruses but still were agglutinable by influenza A/Asian virus. This indicates that the receptor for 433 virus is different from that for influenza, but apparently is the same as that for the two types of hæmadsorption viruses.

RESULTS WITH PATIENTS' SERA

To establish the etiological significance of 433 virus, acute and convalescent phase sera of patients from whom the virus was isolated were tested by hæmadsorption and hæmagglutination inhibition techniques. In all the paired sera tested the titre, by both methods, was at least four times as great in the convalescent as in the acute phase sera.

COMMENTS

On the basis of the evidence obtained the isolated agent must be considered a virus. The virus grows well in monkey-kidney tissue culture and is readily isolated from throat washings.

So far this virus has failed to produce specific cytopathogenic changes in monkey-kidney tissue cultures. However, this is subject to further investigation in the light of the observation made by Pelon *et al.*[6] that cellular changes in case of 2060 virus were affected by the fluid phase of the tissue cultures. It has been established that 433 virus is not related to any of the influenza viruses, NDV, mumps, Copenhagen 222 or hæmadsorption Type II viruses. On the other hand, preliminary work indicates that an antigenic relationship but not identity may exist between 433 virus and hæmadsorption Type I virus. Further investigation of this point is in progress. If the preliminary results are confirmed and further evidence of antigenic relation is obtained, perhaps it would be justifiable to call this virus hæmadsorption Type III, at least for the time being.

Demonstration of antibody response and isolation made from numerous specimens submitted from various parts of the province would seem to exclude a simian origin for 433 virus and to indicate that it played an etiological role in this rather extensive outbreak of influenza-like illness.

It is of interest to note that in one case the virus was isolated on two different occasions, three weeks apart, from a patient whose convalescence was slow.

Detailed study of this virus is in progress and the results will be reported at a later date.

SUMMARY

During the recent outbreak of influenza-like illness in Ontario, a hæmadsorption virus was isolated. This virus was found to be different from any of the influenza viruses, NDV, mumps, Copenhagen 222 and hæmadsorption Type II viruses. Further, it has been established that it is serologically related to but not identical with hæmadsorption Type I virus.

The authors wish to express their thanks to many physicians, medical officers of health and members of the medical units of the armed forces for their co-operation in supplying specimens, sera and clinical data.

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*Vario is specific antisera were kindly supplied by the following investigators: Influenza antisera for PR8, FMI, A/Asian Japan 305, Lee, Swine and NDV by Dr. J. Crawley of the Connaught Medical Research Laboratories; antisera for influenza C and D/Sendai and mumps by Dr. F. P. Nagler of Dominion Virus Laboratories; antiserum for Copenhagen 222 by Dr. K. B. Petersen of the Statens Seruminstitut and antisera for hæmadsorption Type I and II viruses by Dr. R. J. Huebner of the National Institute of Health.

THE COMMON BILE DUCT

The common bile duct was measured with calipers in 112 patients operated upon at the Mayo Clinic for disease of the biliary tract. The diameter of common ducts containing no pathological changes varied from 4 to 17 mm. and averaged 8.85 mm. Ducts containing stones varied in diameter from 7 to 17 mm. and averaged 10.90 mm. The largest duct sizes were noted in cases of obstructive jaundice due to carcinoma of the ampulla of Vater or pancreas. It is concluded that duct size alone is not a reliable sign as to whether or not the common bile duct contains stones.—D. O. Ferris and J. C. Vibert, *Ann. Surg.*, 149: 249, 1959.

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MEDICINE AND FITNESS

As we go to press, the cohorts of Canadian medicine are converging on the dignified old city of Edinburgh to begin the final stage of this year's tripartite Annual Meeting. After a week of social and scientific activity so intense that it is difficult to see how it could be added to, the blissfully exhausted participants will return to what the Scots call their old clothes and porridge, with a sense that they have witnessed a unique year in the history of the Canadian Medical Association.

The second act of this three-act spectacle is already behind us, for on Tuesday June 30, the Association installed its President for the year 1959-60 at a ceremony in the Royal York Hotel, Toronto. The ceremony was brilliant, colourful and impressive, but it was prevented from descending the slippery slope to pomposity by the refusal of the chief participants to put on the masks commonly worn on such occasions. Indeed, the first prize for dispelling boredom and dreariness from the proceedings must be given to our new President, His Royal Highness, The Prince Philip, Duke of Edinburgh. Those who know of His Royal Highness's record as an orator came to the ceremony with pleasurable anticipation, and they were not disappointed. It is true that he paid medicine in general and the Canadian Medical Association in particular those compliments which tradition and courtesy require on such occasions, and in so doing revealed more than a nodding acquaintance with the Association's history and record. But having done this, he then avoided the trap of attempting to spread jam on top of the butter and took the Association to task politely but firmly for certain omissions in their program.

We have recently been told of a successful Scottish immigrant to the United States who suddenly abandoned a life of luxury to take his children back to Scotland where they could obtain "the hardship to which they were entitled". There is little doubt that Prince Philip's experience as a schoolboy in Scotland at the famous Gordonstoun School has given him a healthy contempt for luxury and ease and an equally healthy regard for physical and mental fitness. It came as no great surprise therefore to find in his speech a castigation of our affluent society and an exhortation to seek once more the physical fitness and its associated mental toughness which our forefathers took as a matter of course and which so many of our urban population have now cast aside.

But Prince Philip is sufficient of a doctor to follow diagnosis with a prescription, and in this prescription—a drive in Canada to provide more adequate facilities for physical exercise for both children and adults—he involved the Canadian Medical Association. It was his view that, as doctors, we should not concern ourselves solely with healing the sick, but should make some effort to raise the general standard of fitness in the population. In his suggestion that the Canadian Medical Association should work with all other bodies in Canada trying to promote this aim, we cannot but concur; in our defence, however, we should point out that a month previously the Council of the Canadian Medical Association had in fact debated this very theme.

While agreeing wholeheartedly with the concept that physical fitness and mental fitness are the *concern* of the medical profession, we do sometimes wonder to what extent they are a *responsibility* of our profession. A great number of demands are made upon our profession nowadays to show leadership and take the initiative in reforming society. We are required, for example, to deal with the growing army of alcoholics in our midst and to dissuade the young from the abuse of tobacco. We are expected to stop executives from killing themselves with overwork and overeating, to transform homosexuals into heterosexuals and to change sexual offenders, by surgery or psychiatry, into law-abiding citizens. The editor of a learned contemporary has recently requested us to assist in the abolition of boxing, and some think that we should take the lead in stamping out that other form of slaughter, the automobile accident. Now all these problems certainly have a medical angle, but we can scarcely be expected to deal with them alone. We have the good of the people at heart, but what if they do not want to be done good to! If people want to get fat and lazy, or drink themselves to death or hit each other, what are the limits of our responsibility to them?

Returning to the question of physical fitness, perhaps the answer to the question is supplied by Prince Philip's own background. "Get them young and keep them moving," should be the slogan. We must abandon the system of trying to produce a few stars in the schools, and see that every child in Canada is compelled to participate in an adequate program of physical training. This is a goal towards which we could all work and it's a lot easier than trying to wean middle-aged executives from their office chairs and their martinis or to give psychotherapy to idle juvenile delinquents.

Editorial Comments

ACQUIRED "IMMUNITY" IN TUBERCULOSIS

The problem of artificially produced immunity in human tuberculosis is an extremely important one, the discussion of which is always timely. At present, an agent is available, the administration of which is generally agreed to result in a degree of active immunity against tuberculosis. The objections to the mass utilization of BCG as an immunizing agent against tuberculosis have little to do with the question of its power to produce the desired result. Rather, they are based, firstly, on possible danger attendant on its use; secondly, on loss of the efficacy of the tuberculin test as a screening procedure; and finally, but to a much lesser degree, on the suggestion that the immunity thus artificially produced cannot be as potent as that resulting from a naturally occurring primary infection.

It would appear that, were there available an immunizing agent without the capacity of multiplying in the tissues (and therefore without danger) but still possessing immunogenic properties, the other objections to mass immunizing programs might lose some of their validity. It should, of course, be understood that, in the case of BCG, multiplication is deemed necessary to the immunological process unless large numbers of organisms are used.

In 1955, Vischer and associates[1] isolated a pleomorphic organism from mouse brain, which they tentatively called *Mycobacterium X*. The pathological changes induced in mice by this organism were described as minute proliferative granulomas without caseous necrosis. Acid-fast organisms could readily be demonstrated within cells, but they were usually single and never formed compact colonies such as are found in most tissues infected with a virulent avian strain. It was suggested by these workers that *Mycobacterium X* represents an attenuated type of avian tubercle bacillus; and, in tissue culture experiments, it was noted that attenuated and virulent tubercle bacilli were inhibited within monocytes derived from guinea pigs which had been infected with *Mycobacterium X*. The findings suggested that *Mycobacterium X* has immunogenic properties, and, since there was no conclusive histological evidence for multiplication of this organism in mouse tissues, it was considered that a study should be undertaken to determine the relationship between the immunogenic capacity of this mycobacterium and its behaviour in the tissues.

In an attempt to clarify these points, groups of mice were injected intravenously with cultures of *Mycobacterium X;* at various intervals, the animals were killed and the numbers of viable organisms were determined in the liver and spleen. It appeared clear that the bacterial population remained stable for several days and then began to decline slowly.

Next, the effect of vaccination was determined upon the bacterial population within pulmonary lesions after challenge. In this portion of the study, mice were challenged with a number of H37Rv bacilli which caused a slowly progressive, but not fatal, infection. The mice were killed five weeks after infection, and sections were prepared from the lungs. The bacterial population was established by counts, and the histological findings were evaluated. It was clear that lesions were less frequent and smaller in the vaccinated animals than in controls.

In addition, a large dose of H37Rv infection in control animals was found to be uniformly fatal, while most animals previously "immunized" with *Mycobacterium X* survived the otherwise-fatal dose of H37Rv. Again, in the presence of a rapidly progressive mouse infection with certain other strains of tubercle bacilli, the results indicated that *Mycobacterium X* was an effective protective antigen.

The present authors consider that the results presented in their paper[2] are evidence that *Mycobacterium X* is an effective protective antigen in mice and induces in them a state of increased resistance to a challenge infection with human or bovine tubercle bacilli. The degree of protection achieved was apparently close to that usually obtained after vaccination with BCG, irrespective of whether the infection was extremely virulent and progressive, or attenuated. More significant is the fact that the findings corroborated previous suggestions that *Mycobacterium X* does not multiply to any measurable extent in the tissues of the mouse.

It would thus appear that *Mycobacterium X* fulfils, at least in mice, the combined criteria of immunogenic effect and lack of multiplication in the tissues, which of course is not the case with BCG. Clearly, this organism deserves further investigation, particularly with a view to determining whether the striking results so clearly demonstrated in animals can be duplicated in humans.

S. J. SHANE

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MEDICAL AUDIT

Tissue committees are now functioning in many Canadian hospitals. Usually, they have been formed at the suggestion of the Accreditation Committee inspector and they try to evaluate the standard of patient care in their own centres. Most concern is concentrated on what goes on in the operating rooms: the most obvious place where harm could be done and where the patient is most vulnerable to accidents, lack of skill or slips in technique. Differences in preoperative, pathological and postoperative diagnoses are scanned, wound infection rates are studied, morbidity and mortality statistics are evaluated and compared with whatever statistics can be culled from the literature and the few books written in this field. But new techniques and new drugs and new concepts of operating room and hospital building and equipment and, above all, a steady increase in the quality of surgical training and the standards of surgeons practising have been so rapidly improving these

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statistics that there is a need for more articles on the results of "medical audit".

Once it was said that if the financial records of a hospital were audited as casually and as ineffectively as the quality of its patient care, the administrator and the governing board would probably land in gaol. But the problems of the tissue committee are great. It is easy to stop any rascal, any unethical or conscienceless practitioner who might get into the hospital for a fleeting visit. The wound infection rate soon remains below the accepted minimum, the number of laparotomies without preoperative diagnosis becomes small, the removal of normal organs disappears, the operative mortality appears commensurate with the magnitude of the operation and the lesion attacked, but the tissue committee remains unsatisfied. It is a common experience that within a year or so of setting up the committee the improvement in practice as shown by the statistics studied is very great, and a plateau is reached. The knowledge that such a committee of his colleagues is there seems to make each doctor using the hospital search for his own weaknesses, and this is the most satisfactory result of medical audit. And since the first requirement of the committee is adequate records, the improvement in patient care is much greater than would result simply from the discovery of the complications or accidents or mistakes that happen to be picked out by the committee.

A review of the results achieved by the general surgical audit in the Royal Newcastle Hospital in New South Wales illustrates the value of such a careful self-examination by a hospital staff committee. It is written by John Smyth,[1, 2] who states that the philosophy of an audit committee should be the search for perfection. Some complications such as the burst abdomen are too rare to be worth tabulating in their experience, but the reporting of infected wounds is very closely watched. In this Australian hospital, an infected wound is one in which there is any purulent discharge, even a bead of pus from a stitch-hole, and if the surgeon has not written a note on the chart that the wound healed cleanly, it is assumed that it was infected! It was found that the counting of undesirable features directs attention to the more common risks. Mortality is defined by the statement that every patient is either discharged from hospital or dead. Infected wounds, pulmonary complications, and such hazards inherent in surgery as incorrect diagnosis, uncertainty as to indications for operation, and failure to find a lesion at operation were the most usual topics for the monthly surgical audit meeting.

As John Smyth remarks, a medical audit is not a witch-hunt but the attempt to highlight any weak points that can be found in the care of patients. Medical auditing is directed toward the evaluation of clinical practice rather than clinical practitioners. Canadian surgeons and their patients would benefit by such reports from Canadian committees about their work.

BURNS PLEWES

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VACCINATION AGAINST WHOOPING-COUGH

The Final Report to the British Whooping-Cough Immunization Committee of the Medical Research Council has recently been published in the *British Medical Journal*.[1] The results are reported of field trials involving seven different whooping-cough vaccines which were used on a total of 13,029 children subsequently followed up for 2-3 years. A table shows the details of the seven vaccines which were all prepared in England except for Pillemer's antigen. A further table shows the similarity of the groups tested in trials. Although the antigen extracted from *H. pertussis* by Pillemer *et al.* was more effective in its protective action than the whole bacterial vaccine, it caused more reactions. A pertussis vaccine mixed with diphtheria toxoid (F.T.) was similar in its protective action to pertussis vaccine alone. The diphtheria antitoxin response in children receiving three doses of such a mixed vaccine was slightly less than in another somewhat older group who received 2 doses of diphtheria P.T.A.P.

Assays of the vaccines for their protective potency by the intracerebral mouse-protection test showed a high degree of correlation between the potency of the vaccines in protecting mice against intracerebral infection and their ability to protect children against pertussis. This is a confirmation of previous observations and indicates that only those vaccines which have been shown by this mouse-protection test to have adequate potency should be used in whooping-cough prophylaxis. The antigen fraction produced by Pillemer *et al.* protects mice against intracerebral pertussis infection but produces a poor agglutinin response in mice. It was tried in 4500 children and shown to be able to induce a high degree of immunity, but the agglutinin response was less than that produced by whole bacterial vaccines with equally protective properties. A British standard pertussis vaccine has been prepared from one of the batches of vaccine giving good protection in the field trials, and it will now be possible to ensure in Britain that vaccines will produce substantial protection against whooping-cough. Commenting on the work of the committee on whooping-cough, the editor of the *British Medical Journal* has the following to say: "In view of the concern now being expressed about complicated immunization schedules for young children, it is gratifying that these trials also proved the combined diphtheria-pertussis vaccine to be as effective as the pertussis alone." The trials showed that the attack rate in inoculated children can be as little as 4% of that in the uninoculated, and it is not too optimistic to expect a protection rate of 90%. If widely carried out, immunization should reduce the disease in the next few years to a small fraction of its present incidence.

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Medical News in brief

FATIGUE FRACTURE OF THE PELVIS AND LEG

Fatigue fracture or march fracture is a condition most commonly seen in recruits suddenly subjected to heavy physical training. Wang and his colleagues (*New England J. Med.*, 260: 958, 1959) have collected a series of 97 cases of fatigue fracture of the pelvis and lower limb in 83 patients observed in a U.S. army hospital. The fractures commonly occurred in recruits four or five weeks after the beginning of basic military training and were strikingly frequent in midwinter when heavy clothing and boots were worn. No patient had a history of acute trauma and all were in excellent health. The preliminary symptom was aching pain in the involved bone, the pain being constant and dull and promptly relieved by taking the weight off the limb. In fatigue fracture of the pelvis, the pain was often perineal and aggravated by forceful abduction and adduction of the thighs. Of great diagnostic interest was reproduction of pain at the fracture site by heavy percussion of the ends of the long bone or heel. Point tenderness at the fracture site was also elicited. In fatigue fracture of the tibia, pretibial œdema was common. A large mass of callus was often palpable late in the disease.

Of this series, 75 fractures occurred in metatarsal bones, six in the os calcis, eight in the tibia, four in the femur and four in the pelvis. Since radiographic findings may not be sufficiently developed in early fatigue fracture to be recognized, it is extremely important to re-examine the involved parts two or three weeks after the initial x-ray examination. Treatment was conservative, usually consisting of absolute bed rest for 10 days with gradual ambulation afterwards, regulated by the presence of pain.

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MYXŒDEMA COMA

That myxœdema can lead to death has been known for many years; during the past few years reports of myxœdema coma have appeared more frequently, indicating that this condition is not rare and that it is almost invariably fatal. Nieman (*Brit. M. J.*, 1: 1204, 1959) reports three cases of myxœdema coma with encephalographic findings. The first patient died 24 hours after admission to hospital in spite of intensive treatment. The second was eventually brought out of coma after three weeks, and the third patient died suddenly after initial improvement. Kelly and Sherk (*Ann. Int. Med.*, 50: 1303, 1959) report another case of coma which did not respond to intensive treatment with tri-iodothyronine via stomach tube, intravenous corticosteroids, and other symptomatic means. The patient died after 40 hours and at necropsy only diffuse degenerative changes of the brain compatible with advanced arteriosclerosis were found. There was no evidence of cerebral thrombosis or infarction. Kelly and Sherk suggested the use of intravenous, rapid-acting thyroid preparations in such cases.

BACTERICIDAL CONDITIONING FOR HOSPITALS

In New York, Hudson and his colleagues (*J. A. M. A.*, 169: 1549, 1959) have investigated the use of long-acting bactericidal agents for reducing the number of pathogenic bacteria in the air of the building. They tried four formulas, incorporated in waxes, floor preparations and air filters as well as sprays for walls, ceilings, floors, laundry and furniture. They found that more than four-fifths of the bacteria in air can be removed by the use of such a combined air-and-fomite system of bactericidal conditioning, using substances which are commercially available and economically feasible. They lay stress on the fact that bactericidal control in hospital does not depend on having a central air-conditioning system, and that bactericidal filtration of air, without inclusion of other measures to deal with surfaces and furniture, is not sufficient for an optimal result.

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TOBACCO HYPOGLYCÆMIA

Since 1946, Berry (*Ann. Int. Med.*, 50: 1149, 1959) has seen 24 patients with tobacco hypoglycæmia. His criteria for this diagnosis were: (1) the use of one or more packages of cigarettes per day; (2) symptoms compatible with the diagnosis of hypoglycæmia; (3) blood sugar below 55 mg. per 100 c.c.; (4) prompt relief by ingestion or administration of glucose; and (5) complete and permanent relief of symptoms with cessation of smoking. Seven typical case reports are presented and glucose tolerance curves showing a tendency to hypoglycæmia are given. The symptoms are described and the improvement in the glucose tolerance test following abstinence from smoking is also shown. In discussing the pathogenesis of the hypoglycæmia in these patients, the author suggests that smoking may stimulate pancreatic island hypertrophy. He suggests that before resorting to surgery for possible islet-cell tumour in smokers with hypoglycæmia it would be reasonable to wait for some days or weeks for the hypoglycæmia to subside after cessation of smoking.

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SEX AND SURVIVAL IN HUMAN MELANOMA

Of a total group of 871 cases of melanoma, 439 grouped by site (ocular or cutaneous), sex and age were studied by White (*New England J. Med.*, 260: 789, 1959). Distribution of melanoma was found to be roughly equal in the sexes, but the survival rate was better in females than in males. Females with melanoma have a greater chance than males of living for five years, and the prognosis for females surviving beyond the five-year period is even more striking. This improvement in five-year survival in both sexes is less in the aging than in the younger group. Although pregnancy may adversely affect the prognosis, this has not been definitely proved by statistical study. The variation in behaviour of melanoma at times of hormonal upheaval in human beings, together with the better survival rate in females than in males, suggests the possibility that melanoma is under some sort of hormonal control.

(Continued on advertising page 38)

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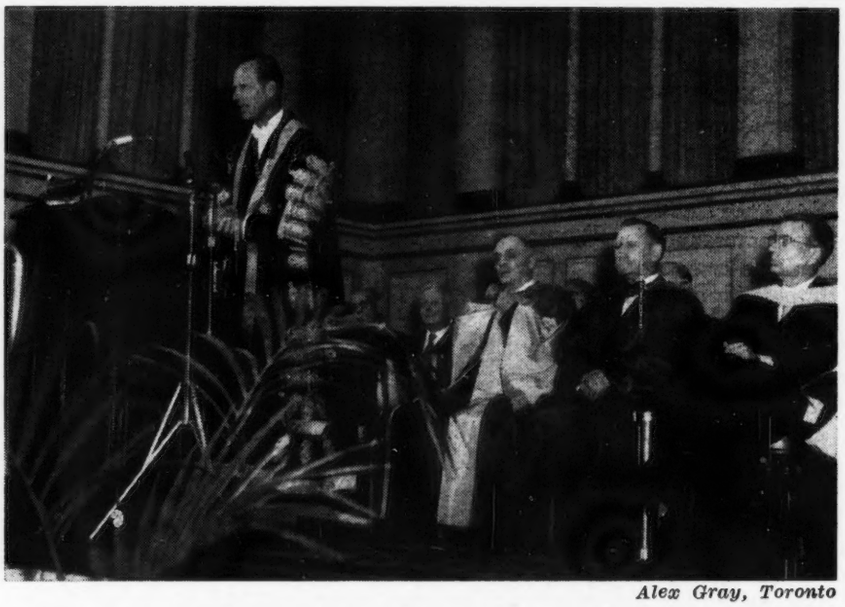
Association Notes

INSTALLATION OF THE PRESIDENT

For the first time in the history of the Canadian Medical Association, a member of the Royal Family was installed as President. This brilliant ceremony took place in the Royal York Hotel, Toronto, on Tuesday, June 30. In the presence of several hundred doctors and their wives, His Royal Highness, The Prince Philip, Duke of Edinburgh, who was in the robes of the Chancellor of Edinburgh University, was invested with the presidential badge. Special guests on the platform at the installation ceremony included Sir Arthur Thomson, of Birmingham, President of the British Medical Association; Dr. Louis M. Orr of Orlando, Florida, President of the American Medical Association; and Dr. Emile Blain of Montreal, President of l'Association des Médecins de Langue Française du Canada. The invocation was given by the Right Reverend F. H. Wilkinson, Bishop of Toronto.

The outgoing president, Dr. A. F. VanWart of Fredericton, welcomed the participants and mentioned a few highlights in Prince Philip's career. In particular, he stressed the Prince's service in the Royal Navy, where his mind developed the scientific and technical bent which is his strongest intellectual trait. The Navy had provided, said Dr. VanWart, "the exacting demands of a great service" which the Prince's Scottish headmaster had specified as requisite for the full development of his character and temperament. Dr. VanWart also referred to the Prince's interest in the provision of playing fields and in the advances in science and technique.

The Presidential chain of office was then transferred to Prince Philip by the C.M.A. Chairman of Council, Dr. Norman H. Gosse of Halifax.



Alex Gray, Toronto

The newly installed President, making a vigorous onslaught on "sub-health", has the attention of Drs. A. F. VanWart, N. H. Gosse and Louis Orr, President of the American Medical Association.

When His Royal Highness addressed the gathering after his installation, he made a characteristically vigorous speech. He said that he regarded the invitation to become President as a great honour and privilege and as a gracious gesture on the part of the medical profession to their victims. His presidency would enable him to say something nice to the profession as a whole on behalf of the many patients who owed so much to the tireless and selfless work of doctors and nurses. After mentioning some stalwarts of the C.M.A., including his predecessor as joint B.M.A.-C.M.A. President, Dr. T. C. Routley, he paid a tribute to the achievements of the Canadian Medical Association in such activities as the promotion of high standards of hospital practice, the identification of Canadian hospitals approved for internship, the approval of schools for laboratory and radiological technicians, the promotion of health education of the public, the support of international medicine through the World Medical Association, the World Health Organization and the British Commonwealth Medical Conference, co-operation with governments in the recent hospital insurance plan, the promotion of health insurance through voluntary plans of prepaid medical care, and the education of medical students. He felt that the general public should be given every chance to know that the Canadian Medical Association was not simply a trade union for doctors but an organization constantly rendering useful and practical service to the entire population.

He felt confident that his Deputy, Dr. Kirk Lyon, would perform the Duke's duties to everyone's entire satisfaction. Speaking in French, he expressed his pleasure at seeing a delegation from the French-speaking physicians of Canada and extended his felicitation to Dr. Renaud Lemieux on the occasion of his presidency of the World Medical Association.

Referring to changes in the modern world, His Royal Highness said that we must distinguish between the causes of change and the consequences of change. Thus for example the spectacular reduction in death rates in underdeveloped countries had been caused by medical science, and as a consequence of this the pressure on the natural resources of the world was assuming gigantic proportions. Quoting some figures for hospital admissions in Canada, he pointed out that in spite of everything it would not be reasonable to assume that the general level of health was improving. The causes of this state of affairs were widespread but not far to seek; they included urban living, lighter work, increased leisure, more sedentary occupations, a higher standard of eating and the very powerful assistance to survival of the weak.

Turning to the world of sport, he noted that with a few exceptions, Canada's achievements in sports and games were hardly in keeping with a country which claimed almost the highest standard of living in the world. This very standard of living, of which the country was so proud and which seemed to be a goal of all the nations of the world, was having the same effect upon the community as a plaster cast had on the

muscles of the body. Quoting from the report of the Sports Governing Bodies of the United States in 1955, he noted that 78% of American children tested failed with a test for minimum muscular fitness, as against 8½% of European children, and that 54% of children first entering school were unable to pass these tests. This suggested that nearly half the younger population was already in a state of sub-health. The speaker then quoted further from the 1958 paper read by Dr. Doris Plewes, Consultant to the Office of the Deputy Minister (Welfare) in Canada, in which she referred to the startling inadequacies as regards provision for physical education in Canadian schools. She had said that there was reason to believe that despite the greatly lowered incidence of communicable diseases and improved standards of living, present-day children lacked the sturdiness and staying powers of the pioneers. The speaker commented, "I would only add that there is also a connection between emotional instability, low-level physical efficiency and delinquency. The lawless and the listless are equal menaces to society."

"The question I want to ask is this. Is the medical profession content only to fight disease and disability and accept the negative definition of health as someone who is not actually ill? Or is it also going to take notice of the state of sub-health which exists?" He then drove his point further home by referring to the Act of Incorporation of the Canadian Medical Association, from which it would seem clear that the Association was charged to deal with questions of health and fitness. In the speaker's opinion, there were two main ways of fighting sub-health. The first was based on the ancient maxim that prevention is better than cure and the second on the variant that if a cure works it will work even better as a preventive. The first thing to do was to see that all children from an early age received regular physical instruction by properly qualified teachers.

Alex Gray, Toronto

This particularly happy picture of the new President, wearing the chain of office of the President of the C.M.A. and the robes of the Chancellor of the University of Edinburgh, includes representatives of both Associations. They are (left to right): the Hon. Herbert Bruce, Senator Joseph A. Sullivan, and Sir Arthur Thomson, President of the British Medical Association, soon to hand over his presidential chain to Prince Philip.

He then referred to various schemes worked out by laymen such as the Outward Bound schools and The Duke of Edinburgh's Award named for him, but pointed out that these touched only a small fraction of the population. The widespread realization of the seriousness of this problem of sub-health was essential, or it would get worse. He added that the provision of useful physical activities for adults was also essential.

In his peroration, the Duke said that he would like the Canadian Medical Association to make its own inquiries into the state of the health of the nation and to give support and encouragement to all organizations working for better health and fitness, and also to make a wholehearted effort to reverse the trend of the statistics which at present show only more beds, more mental cases and more unfitness in children and adults. He said "One thing I beg of you—don't go away from here saying 'This has got nothing to do with me and anyhow I'm fully occupied with curing disease' because you know it isn't true. You cannot afford to ignore the facts and still maintain that you are in the least bit interested in health. Strong words perhaps, but you took a risk; you asked for it when you invited a layman to be your President."

"The Canadian Medical Association has a tremendous record of service to the community and I firmly believe that your opportunities for service in the future are greater than ever."

After the enthusiastic applause which followed this fighting speech had subsided, the Past-President's badge was presented to Dr. Arthur F. VanWart, and after the presentation of the platform party and their ladies to His Royal Highness in the Ontario Room, a C.M.A. luncheon was served in the Canadian Room, with the new President in the chair. The Royal chairman spoke briefly at the luncheon, including in his

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remarks a charge to Dr. Kirk Lyon, his Canadian Deputy, to represent him in all matters connected with the presidency and handing to Dr. Lyon the President's chain for safe-keeping and use.

GENERAL PRACTICE

THE CONTROL OF ACID IN THE DUODENAL ULCER PATIENT*

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WHILE MANY THEORIES have been proposed to explain the development of duodenal ulcer, only one has a large body of evidence in its favour. Patients with duodenal ulcer have increased duodenal acidity, as shown by aspiration[1] and *in situ* pH electrode[2] techniques. If this can be controlled or corrected, the ulcer will heal and stay healed.

What is the cause of the increased duodenal acidity? The most obvious explanation of course is that it is secondary to increased production of gastric acid. It has been apparent for decades that patients with duodenal ulcer secrete more than the average amount of acid, but the possibility exists that this is secondary to the development of the ulcer. Other possibilities are:

1. Inadequate duodenal, biliary or pancreatic secretion.
2. Inadequate mucus production.
3. Rapid gastric emptying of acid chyme.

In duodenal ulcer, gastric emptying is actually delayed, and there is no evidence that production of the protecting factors is deficient.

We must conclude then that the increased duodenal acidity is secondary to increased gastric acidity. This is not because the parietal cells of these patients secrete an acid of increased concentration, for it has been shown that the acid secreted by all parietal cells is of a fixed concentration, which can be expressed as 0.16N, 0.5%, or pH 1.[3] The increase is only quantitative. Not only do patients with duodenal ulcer have higher resting and nocturnal acid levels, but they also respond to the stimulation of food hypoglycæmia, and histamine to an exaggerated degree.[4] Why is this so?

Patients with duodenal ulcer have an increased number of acid-producing parietal cells,[5] and it is tempting to conclude, as has been done, that this is the basic explanation.[6] However, it has also been shown that parietal cells will multiply in response to stimulation,[7] so that this increase in parietal cell population could be secondary to increased stimulation. Another possibility is that mechanisms which normally terminate acid production following stimulation fail to do so. Thus excessive acid production may be the result of excessive stimulation or inadequate inhibition. The normal stimulatory mechanisms via the vagus, antrum and intestines are well established.[3] These mechanisms operate to ensure an adequate production of gastric juice for digestion, but if this hypersecretion was not terminated when no longer required, we would all develop duodenal ulcer.

Hypersecretion is terminated by mechanisms in the antrum and duodenum when the acidity becomes sufficiently high. Dragstedt[8] demonstrated in the experimental animal that acid in the antral region suppressed further acid production, presumably because gastrin was no longer produced under these conditions. We have suggested on the basis of further experiments that an active inhibitor substance is produced by the antrum[9] which will inhibit the acid produced in response to intestinal and vagal stimulation.[10, 11] The relationship between the vagus and antrum is not clear, and there are several other controversial points which remain to be clarified.[12]

This rather complex control of gastric secretion must be kept in mind when planning medical and surgical therapy for these patients. Only vagal stimulation can be altered pharmacologically, but an attempt can be made to neutralize, buffer or dilute the excessive volume of acid. Of the many commercial anticholinergic agents, none appears to be superior to atropine.[13] None of the neutralizing agents can significantly lower gastric pH for more than a short time, and there may be a marked increase in acid production subsequently (rebound). Bearing in mind the normal mechanisms which stimulate and inhibit the secretion of acid, it can be appreciated that food will neutralize acid, but also stimulate its further production. Fat might be expected to be superior in this respect, as it delays gastric emptying and inhibits acid production. More important than the avoidance of certain foods is a program which keeps food in the stomach at all times. Although alcohol, tobacco and coffee should be avoided, it is not necessary to follow too strict a diet. In the prevention of an exacerbation, patients generally place these three major factors in the following order:

1. Prevention of fatigue and "stress".
2. Frequent snacks.
3. The use of medication.

How successful is medical therapy? The acute bout can almost always be relieved. Whereas 90% of patients without any care will have an ulcer recurrence within a year, only 10% will do so if they follow a good regimen. However, even with the best of treatment the recurrence rate in this same group will rise year by year, and we cannot prevent the occasional recurrence in more than half these patients. Of this group, however, 80% will be able to carry on without surgical care, in contrast to only 50% of patients who fail to follow a proper regimen.

SURGICAL TREATMENT

Before considering the indications for surgical treatment, let us look at the results of surgery in duodenal ulcer. Historically, this has been the search for an operative procedure with a low ulcer recurrence rate and minimal postoperative sequelæ. During this search, almost every possible combin-

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ation and permutation of operations on the upper gastro-intestinal tract has been developed. Because of the excessive mortality of gastric resection, drainage procedures such as gastroenterostomy or pyloroplasty were generally employed until the 1930's, when it became obvious that these procedures were followed by a prohibitive ulcer recurrence rate. By this time it was possible to perform gastric resection with a reasonable mortality, and the problem of ulcer recurrence was successfully solved by a 75% gastric resection. However, as more and more of the stomach was removed to reduce the incidence of stomal ulcer the incidence of postoperative sequelæ rose, and it was accepted that ulcer recurrence could not be kept below 5% without accepting a significant incidence of postoperative problems. When vagotomy was introduced by Dragstedt in the 1940's, it was hoped that the addition of vagotomy to a less radical gastric resection, or its combination with a drainage procedure, would solve both problems.

Although there are now 10 commonly employed procedures, it is fair to say that none completely satisfies all the criteria of a low operative mortality, a low ulcer recurrence rate and minimal postoperative sequelæ. For this reason it is necessary to limit surgical treatment to those patients seriously handicapped by their ulcer disease. Severe pyloric obstruction, perforation, and hæmorrhage in certain cases are definite indications for surgical treatment. The majority of patients, however, are suffering from various degrees of pain, vomiting and bleeding, under varying degrees of medical control. Intractability as an indication for surgery is a relative matter, and it is difficult to define the proper indications for surgical treatment in such a situation. Ulcers in such patients can be divided into several categories:

1. Those that heal and stay healed with no medication or diet.
2. Those that heal and stay healed with medication and dietary control.
3. Those that heal but recur occasionally (annually or semi-annually) and only receive care during exacerbations; the patient is not seriously affected in day-to-day living.
4. Those that heal but recur occasionally (annually or semi-annually) in spite of continuous medication and diet; the patient is not seriously affected in day-to-day living.
5. Those that heal but recur frequently (more frequently than semi-annually, or remain chronic) — care only during exacerbations; the patient is seriously affected in day-to-day living, and cannot (occupation or obesity) or will not (alcoholic, vagrant, psychotic) follow advice at all times.
6. Those that heal but recur frequently (more frequently than semi-annually, or remain chronic) in spite of good care; the patient is seriously affected in day-to-day living.

Generally the first three groups are definitely not candidates for surgical treatment, whereas the last two almost invariably are. Whether or not those in Group 4 are advised to have surgery will depend on their age and general condition, the length of their ulcer history, their occupation and the extent to which they are economically disabled, their facilities for good medical therapy, and their attitude towards their continuous dietary restrictions and medication. If a completely satisfactory operation was available for duodenal ulcer, there is no doubt that this group, as well as selected cases in Group 3, would become candidates for surgical treatment.

As well as mortality and recurrent ulceration, the complications following the surgical treatment of ulcer are postcibal dumping, postcibal hypoglycæmia, bilious vomiting, diarrhœa, food intolerances, and inability to gain weight. If leading questions are employed, at least 75% of postoperative patients will admit to one or more of these symptoms early in their postoperative period, but fortunately the side effects diminish in frequency and severity until at the end of two years only 40% admit to residual symptoms. Only 2 to 3% are permanently affected by severe postoperative sequelæ which interfere seriously with their day-to-day living and economic potential. The relative incidence of each of these postoperative problems varies with the choice of operation, but no procedure is free of them. Inability to gain weight with consequent fatigability is more common after radical gastrectomy. In our own hospital Dr. J. A. L. Gilbert has recently found that 20% of our postoperative patients were 20 lb. or more below their preoperative weight on a two-year follow-up. In spite of this, 90% felt that the operation had been successful. This, of course, reflects a careful selection of patients for surgery.

Treatment of Postoperative Complications

The most frequent cause of death is duodenal stump leakage, and this usually reflects failure on the part of the surgeon to recognize a duodenum which could not be safely closed. As Sir Heneage Ogilvie has sagely remarked, "The best way to prevent milk from turning sour is to leave it in the cow." Ulcer recurrence generally reflects an inadequate primary operation, but it is not necessarily an indication for immediate re-operation. A trial of medical therapy is occasionally successful.

The symptoms of epigastric fullness, nausea, sweating, palpitation and weakness that occur within an hour after a meal fall within the category of postcibal dumping. These symptoms are due to jejunal distension secondary to rapid gastric emptying and the added transfer of fluid from the intravascular compartment to the hypertonic contents of the upper jejunum. These symptoms are almost invariably present to some degree after gastrectomy, and dry small meals taken at frequent intervals should be continued as long as symptoms persist. Fluid should not be taken until one-half hour after the meal, and the diet should be high in fat and protein and low in carbohydrate. Symptoms can also be reduced if the patient lies on the left side immediately after meals, or if symptoms are severe the meal can be taken in this position.

Postcibal hypoglycæmia occurs more than an hour after meals, and although its mechanism is quite different the symptoms resemble those of postcibal dumping. Its symptoms are those of

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hypoglycæmia, presumably due to rebound following the rapid absorption of carbohydrate during the early postprandial period.[14] Symptoms may be reduced or prevented by the use of ephedrine grain ½, 30 minutes before meals, a diet high in protein and low in carbohydrate, and the administration of sugar for the relief of symptoms if they appear.

Bilious vomiting occurs if bile in large quantities persists in the stomach. This is tolerated very poorly, and leads to vomiting which relieves the symptoms. If it is severe and persistent, the anastomosis may have to be modified surgically. Diarrhœa is more frequently seen after vagotomy; its etiology is unknown, and effective therapy is not available.

The problem of food intolerance is not a serious one, but difficult and intractable symptoms are occasionally seen after gastrectomy that do not follow any of the above patterns. These are generally psychogenic in origin, and may be so troublesome that psychiatric help is necessary.

Inability to gain weight, with subsequent fatigability, is often but not invariably associated with dumping. Although there is excessive loss of fat in the stool after gastrectomy, the essential problem appears to be inadequate oral intake. Therapy should be directed toward a high-fat, high-protein and low-carbohydrate diet with six or more meals a day, and relief of dumping symptoms if these are present.

Microcytic iron deficiency anæmia is common after gastrectomy, whereas macrocytic anæmia is rare, particularly after subtotal gastrectomy. When macrocytic anæmia develops after less than a total gastrectomy, one can be almost certain that it would have done so without surgery.

SUMMARY

Duodenal ulcer is due to increased duodenal acidity secondary to an increased production of hydrochloric acid by the stomach. This increased production may be due to a constitutional increase in parietal cells, or to a secondary increase in parietal cells. If this is secondary, it may be the result of increased stimulation or a failure of the normal inhibiting mechanisms.

The selection of patients for surgery on the basis of intractability of the lesion is considered, and the present limitations of surgical treatment are discussed. Postgastrectomy syndromes are described briefly and their therapy is outlined.

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UNITY AMONG THE GENERAL PRACTITIONERS OF CANADA

THE NEW PRESIDENT of the College of General Practice of Canada, Dr. M. E. Hobbs of Millbrook, Ontario, gave an inspiring address to the Ontario Chapter of the College on May 28, in which he discussed the responsibility of the College in creating unity among the general practitioners of Canada. He was particularly concerned, as many others are, with the intrusion of third parties in the traditional relationship between doctor and patient, and felt that too many practitioners took the easy way out by ignoring these issues. In recent decades, medicine had changed not only scientifically but also in relation to social and economic changes.

The present public demanded insurance and security against all sorts of risks, and was better informed on these matters than even 25 years ago. A combination of curiosity in medical matters, anxiety about the future and too much leisure time tended to create unstable individuals with psychiatric problems.

Dr. Hobbs noted the increasing complexity of modern medicine, in respect of facilities and equipment and also in respect of paper work and form-filling. He felt that the intrusion of the third party in medicine had made practitioners less satisfied with their work, while the increasing demands of the rest of the population for shortened work weeks and pension plans had produced a tendency in the doctor towards a business rather than an humanitarian approach. The only way to correct this unfortunate situation was to maintain the traditional doctor-patient relationship, with freedom to set fees and retain the incentive of conscientious application to the profession of medicine. The speaker felt that the College of General Practice of Canada had been formed none too soon to save the general practitioner from an ignominious future, and that the College had already accomplished a great deal. It had done much to establish friendly relations between the French-speaking and English-speaking practitioners of Canada and had also accepted the challenge of producing well-trained and highly esteemed general practitioners. But this was not enough; these practitioners required a favourable environment with an atmosphere as free as possible from frustrations created by a third-party intrusion. In conclusion, he felt that the future of general practice in Canada rested largely with the College. This was a challenge which the College had to face.

KNOW YOURSELF

"We must not allow our desire to serve where needed as physicians make us lose sight of the need to protect the people by protecting the profession which serves them." —L. D. Baker, President of the Medical Society of the State of North Carolina, *N. Carolina M. J.*, 20: 174, 1959.

MEDICAL MEETINGS

THE CANADIAN FEDERATION OF BIOLOGICAL SOCIETIES

The Canadian Federation of Biological Societies, which contains the national organizations representing anatomy, biochemistry, physiology and pharmacology, held its Second Annual Meeting in the University of Toronto on June 9, 10 and 11. Almost 200 papers were given, and from these we can notice only a few with possible clinical connotations.

Several of the papers given in the session on *Gross Anatomy and Histology* on Tuesday morning had clinical applications. Forstner of Toronto described his studies of the vascular anatomy of the liver. He had perfused fresh livers with normal saline, injected them with vinylite plastic and corroded them with hydrochloric acid. Others were perfused, preserved and injected with coloured latex. Studies of the specimens revealed a fairly constant vascular pattern of practical importance in surgery. For example, there were nine areas of separate vascular supply on the inferior surface of the liver. He also described the distribution of the portal and hepatic veins, which again showed constant features. Anderson of Toronto called attention to the neglect of autopsy studies of the region of the vertebral artery. He had studied this region in 200 dissecting room cadavers and 124 skeletons of ancient Indians. He noted that changes sufficient to produce occlusion of the artery by pressure from within were common. For instance, the foramen transversarium was very variable in size and shape, and often encroached upon by osteoarthritic lipping. There was a high percentage of malformations particularly affecting the sixth cervical vertebra, though in the Indian collection the seventh vertebra was more commonly affected. Of persons over 35 years old 87% showed evidence of lipping of the vertebral bodies, and in 31% the cervical articular facets were involved. Curiously enough, the much younger Indians had just as much osteoarthritis. There was no correlation between the amount of arthritis and the degree of closure of the foramina, and it seemed that variations in the latter were genetically determined.

Fyfe of Dalhousie University, Halifax, had continued experiments begun by Dr. Trias on the effects of intermittent pressure in rabbits on the knee joint, transmitted by means of femoral and tibial shaft pins, so as to simulate in an exaggerated way the normal intermittent pressure on the knee joint. These studies were of some significance in the genesis of genu valgum because in rabbits under 3 months old, the fibula seemed to act like a bow string and bend the overgrowing tibia. Basmajian of Kingston discussed the factors preventing downward dislocation of the shoulder joint. He had taken electromyograms in a series of healthy students to study muscle activity with the upper limb hanging freely by the side, and discovered that whereas deltoid relaxed rapidly and became inactive supraspinatus continued to show moderate activity, which was accentuated if the subject held a heavy weight or had his arm pulled vertically down. The author believed that downward dislocation of the shoulder joint was prevented by the supraspinatus and also the upper part of the capsule of the shoulder joint. Downward movement of the head of the humerus implied also lateral movement, which was opposed by the muscle and the capsule. This mechanism is a very efficient one. Von Hochstetter made a plea for the use of the anterior part of the gluteal region for intramuscular injection. He took three points, the anterior superior iliac spine, the prominence on the crest of the ilium and the greater trochanter, and injected in the triangle enclosed within them. He claimed that this was a simpler and safer site for injection.

In the section of *Histology and Embryology*, Dr. Murray Barr of London, Ontario, discussed four conditions in which mental deficiency might be associated with aneuploidy or a variation in the normal number of sex chromosomes. The first condition was the Klinefelter syndrome, in which males with small testes, hyalinized seminiferous tubules and abnormally large aggregates of interstitial cells in the testes occasionally showed mental deficiency. These patients had an abnormality of sex chromatin with the chromosome number of 47 instead of the normal 46. A second state of aneuploidy was the Turner syndrome with rudimentary gonads and a chromosome number of 45. Thirdly, it had recently been shown that mongoloids had 47 chromosomes. The fourth type, which Barr himself had worked on, was a condition in which a large proportion of the cell nuclei had two masses of sex chromatin instead of one. In one case studied, the nuclei of cells in all tissues showed the same bizarre pattern as the oral or skin cells; even 80% of the nerve cells showed this anomaly. He had studied five patients in detail, with an intelligence quotient of 30 to 54: two females were normal apart from their mental deficiency, and in the males the testes were normal. If aneuploidy should prove a significant factor in a number of cases of mental defect, it would then become very important to study all the factors concerned with chromosome division.

In the section on *Cancer*, E. R. M. Kay, now of the University of Rochester and formerly at Dalhousie, discussed the scientific basis of an old folk remedy. European folklore has asserted that garlic contains an anti-tumour agent, and Kay has shown that the antibacterial agent in garlic, known as allicin and formed by enzyme action when garlic is crushed, will retard the growth of Ehrlich ascites carcinoma in mice, although it does not cure the condition. The site of action has not yet been determined.

In the section on *Carbohydrates*, Love, Kinch and Stevenson of London, Ontario, described their work on pregnancy in alloxan diabetes in the rat. They found that litters born to diabetic rats were smaller in number and lighter than in controls, but individual pups were significantly heavier, especially if stillborn. When the diabetic animals were treated with insulin, they gave birth to lighter pups. This correlates with figures from New England in which it has been shown that in humans, diabetic mothers treated with insulin give birth to infants weighing less than untreated diabetics do. Adamkiewicz of the University of Montreal had some interesting material on dextran inflammation produced in rats. He showed that this inflammation does not occur when the rat is made diabetic with alloxan, but the inflammation can be immediately restored by giving insulin. McColl of Montreal reported some investigations of tolbutamide and its analogues known as FWH 114 (Stabinol), FWH 116 and FWH 106. Of these, Stabinol had already been investigated in the U.S.A. and the West Indies for a year and found a satisfactory antidiabetic agent in doses of 750

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to 1000 mg. a day. The present studies were done on rats and revealed a higher percentage mortality in females than males. Since the blood sugars were not significantly different, the mortality differences seemed to be due to a difference in hormone balance. This hypothesis was tested by giving rats testosterone or stilbœstrol, and it was confirmed that stilbœstrol increased toxicity greatly while testosterone lowered it greatly; giving insulin simultaneously increased the toxicity in each case. The mode of death was like that in acute hypoglycæmia.

The section on *Cardio-respiratory and Environmental Physiology* began with a film made at the R.C.A.F. Institute of Aviation Medicine, Toronto, showing the effects on human subjects of rapid decompression to hypoxic altitudes. The film was an impressive demonstration of the very small amount of time available to persons undergoing sudden decompression at 40,000 feet before they can adjust an oxygen mask to their faces. Several members of the experimental group were unable to put on their masks without assistance, because convulsive movements and incoordination began within a few seconds. Brent of Toronto stated that cardiac irregularities and premature beats were commoner in subjects put under a double stress with hyperventilation plus G than in those submitted either to hyperventilation or G alone. Fluctuations in heart rate were sudden and enormous and this was apparently not a reflection of cerebral or muscular disturbance, as shown by the absence of such fluctuations in the electrocardiograms of epileptics undergoing convulsions. This cardiac abnormality may be implicated in certain obscure aircraft crashes. Fletcher of Toronto had studied the effects of posture on the speed of cardiac recovery after exercise, and found that pulse rates returned to normal more readily when the subject sat down after exercise than when he stood up or lay down. The return of blood to the heart was a more important factor than any mechanical effect on respiration. Lefcoe of London, Ontario, described the critical analysis of several tests of ventilatory function, including the timed vital capacity, the maximum breathing capacity and the air-flow resistance. His studies showed that both the TVC and MBC were more sensitive as a measure of early impairment of flow than was the resistance measurement. There is however still no infallible test of early bronchial constriction. Lépine of Montreal said that air pilots and industrial workers were sometimes exposed to a hot dry environment and that this had been alleged to have a deleterious effect on pulmonary function. His findings did not agree with this, for subjects placed in a hot room at 118° F. and relative humidity 25 to 30% showed no significant changes in functional residual capacity, vital capacity or gas exchange. An increase in expiratory reserve volume was probably related to decrease in pulmonary blood volume. No doubt exposure to a humid hot environment would have put them under greater stress. Hildes of Winnipeg had conducted experiments on exposure of one hand to cold, and found suggestions that local acclimatization took place in the exposed hand, which after repeated exposure became more resistant to the numbing effect of cold water; this was in part a vascular phenomenon. Hunter of Toronto had studied the relationship of blood pH and glycogen store to recovery from hypothermia induced in rats by cooling under rebreathing conditions. He had imitated the effects of carbon dioxide build-up by producing metabolic acidosis with acetazolamide (Diamox) during cooling. This permitted the revival of animals in which respiratory and cardiac arrest had been produced by cooling to 15° C. and was associated with a higher cardiac glycogen content. Mayer of Kingston, Ontario, discussed environmental factors influencing blood clotting. His studies had indicated that: (1) emotional upset, depression or anxiety, (2) a change in diet to one low in animal fat and high in corn oil, and (3) sudden changes in barometric pressure all contributed to significant variations in the standard clotting time. These observations were important in long-term management of cases with anticoagulants.

Pharmacology Society Symposium

The Pharmacological Society of Canada conducted a symposium on thrombolysins and thromboplastins. Two workers from the Connaught Medical Research Laboratories, Drs. Charles and Painter, discussed thrombolysins. Charles traced the history of the recognition of proteolytic enzymes in the blood, noting earlier work which showed the existence of plasminogen, which could be activated by streptokinase to plasmin and thus be made to lyse clots, though the side effects of fever, etc., made it difficult to use clinically. Substances activating plasminogen were later divided into: (1) activators such as chloroform, trypsin and the activators in urine, blood and milk; (2) lysokinases such as streptokinase, requiring prior activation. Potency of plasmin could be assayed by the amount of casein it hydrolyzed or by other methods. All the evidence pointed to the activation of plasminogen to plasmin as a splitting off of something from the molecule of plasminogen. Obviously the use of a non-antigenic activator would be clinically significant. Painter reviewed the more recent work on plasminogen activation, discussing the physiological activators which fell into two groups: (1) the very specific bacterial activators and (2) the slow non-specific tissue activators or activators in such substances as urine, which are non-antigenic in the same species. In the human, the proactivator under the effect of streptokinase becomes an activator which with further plasminogen forms plasmin. In the first stage of this process, the streptokinase acts stoichiometrically and not enzymatically. Painter considered that urokinase was an excretory form of the tissue cell activator and had studied tissue cultures to see whether they would still contain activators if completely freed from serum. Normal blood has a fibrinolytic activity which varies with the time of day. Capillary dilators, such as nicotinic acid, lead to fibrinolysis by permitting the tissue kinase to permeate through into the vascular system. The plasma contained an antiplasmin, and fibrin also absorbs plasmin; these two facts account for the absence of lysis of plasma proteins in the ordinary blood.

J. F. Mustard of Toronto discussed the role of lipids and thromboplastins in coagulation, pointing out that there was very little factual material on this subject. It had been suggested that the phospholipid, phosphatidyl ethanolamine (PE), is contributed by the platelets to form thromboplastin (T). Others had said that another lipid, phosphatidyl serine (PS), was the essential factor. He had shown in *in vitro* tests that PS did have an anticoagulant effect whereas PE accelerated clotting. *In vivo* he had injected phospholipid

fractions from brain and liver intravenously and found that after injection of PE into the test animal the plasma and serum Christmas factor activity rose rapidly while the clotting time was accelerated. On the other hand, with injection of PS the opposite effect was obtained. Another important question was whether those phospholipids present in butter and eggs might affect the clotting; some said that they did and others disagreed with this view.

After the symposium, J. M. Parker of Montreal described a study made jointly by the C. E. Frosst and Ciba Companies in Montreal on the toxicity of reserpine. He pointed out the difficulties in the way of correlating the results of animal tests of toxicity of a new drug with the clinical toxicity. He discussed the history of studies of reserpine and noted that initially the side-effects had been studied for two months in rats, dogs and monkeys. In man, the important extrapyramidal effects had not been noticed at first. He demonstrated the relationship between the size of the dose, the length of treatment, and the age of the patient with the incidence of serious side-effects, such as depression. However, it might be that the drug simply unmasked latent depressions in predisposed persons. It certainly seemed that with reserpine it would have been impossible to discover the maximum safe dose in man from animal experiments. The chairman, J. K. W. Ferguson of Toronto, pointed out the extreme importance of having more and more studies of this kind carried out.

Endocrines

In the session on *Endocrines*, several papers were devoted to problems related to hypertension. Chappel of Montreal discussed the phenomenon of adrenal-regeneration hypertension occurring after adrenalectomy and unilateral nephrectomy. His studies suggested that the cause of this hypertension was not an increased sensitivity to adrenal steroids. Fraser of Toronto had investigated the role of ovarian hormones in adrenal-regeneration hypertension, and on the basis of his findings suggested that this type of hypertension differs in pathogenesis from that induced by aldosterone. Gornall of Toronto had previously described the development of a mild hypertension when very small doses of aldosterone were administered to rats over a prolonged period. His further studies had supported the view that a chronic and slight excess of aldosterone might be a potentiating factor in the etiology of aldosterone. LaPlante of Montreal showed that in rats suffering from adrenal-regeneration hypertension the aldosterone secretion was negligible and the corticosteroid secretion was lower than normal, but secretion of a steroid complex RT 5 was greatly increased. There seemed to be some basic disturbance in the regenerating tissue but how this produced a hypertension was still unknown. Two further papers dealt with nephrosis. Despointes of Montreal discussed the mechanism by which aldosterone secretion led to œdema in nephrosis produced in rats by aminonucleoside. Kalant of Montreal noted the great difference between the two types of nephrosis produced by aminonucleoside and anti-kidney serum. The former produced a persistent œdema and the latter only a transitory œdema; some factor other than the low albumin level in blood must be responsible for the œdema. It seemed that the anti-kidney serum failed to cause persisting œdema and ascites through its failure to stimulate production of aldosterone.

In the *Pharmacology* session, McLennan of Kamloops described some interesting observations on tick paralysis. The bite of the Rocky Mountain wood tick (*Dermacentor andersoni*) may cause an ascending flaccid type of paralysis in animals and man. Studies by Murnaghan of Ottawa had shown that the paralysis was due to failure of the nerve impulse to liberate acetylcholine at the neuromuscular junctions. This seems to be due to a defect in the release mechanism.

Federation Symposium

On Thursday afternoon the Federation held its second symposium. This time the subject was "The Biological Effects of Ionizing Radiation" with Dr. E. A. Sellers of Toronto in the chair. The first paper was given by Whitmore of Toronto who described the six main variations in ionizing radiation—x-ray, electron, proton, neutron, deutron, and alpha particle—in order of increasing intensity of track, together with shortening of track. Because of the differences in intensity, there was a great variation in the dose of these varieties required to produce a given amount of damage; thus 10,000 to 20,000 electrons might be required to do as much damage as one alpha particle. After discussing the radiation chemistry of water, he noted the anomaly that some types of damage, such as damage to chromosomes, were more efficiently produced by an alpha particle than an electron, whereas damage to viruses was more readily produced by electrons. He noted the effect of oxygen in enhancing the ionizing effect of the sparsely ionizing electron more than the denser neutron. Much more work was needed for an understanding of these basic problems.

The second paper on the cellular approach to radiation was given by G. M. Clark of Toronto who discussed the effects of radiation on the cell. He called attention to the remarkable differences in sensitivity of cells; protozoa would take much more radiation without damage than higher animals, and the different tissue cells differed in sensitivity. There was a decrease in radiation sensitivity with increase in chromosome number. The dose rate was important and the sensitivity of the chromosomes changed during the mitotic cycle. The chromosomes were very sensitive in the stage of interphase and early prophase when they were dividing. Thus irradiated cells in metaphase could continue in their cycle whereas cells at a later stage stopped dividing, hence the increased mitotic index. The inhibition of mitosis depended on the dose and the dose rate; if the radiation dose was given over a very long time it had no effect on mitosis. The speaker concluded by making some reference to his studies of the effects on enzyme reactions in a simple organism.

The third paper was given by Sellers who dealt with the "somatic" effects of ionizing radiation and noted that exposure to ionizing radiation differs from other changes in the environment in that it affects many more cells of an organism. In fact, such radiation affects any molecules along its track, regardless of the molecular structure. In contradistinction to thermal or drug injury, signs and symptoms of radiation injury do not appear at once. Because of the different sensitivities of different tissues one might expect a phasic pattern of injury with various stages of injury and repair going on simultaneously, and this is so. With

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rapid exposure to a high dose of radiation, death was due to injury to the central nervous system; with a lower dose rate the gastro-intestinal tract was affected, and with a still lower dose rate the bone marrow. At first sight it might appear that the actions of ionizing radiation and of drugs were very dissimilar, but analogies existed; for example, amphetamine or chloroform had different toxic actions if given rapidly or slowly, and some drugs were just as toxic on a molar basis as was radiation. Most of the somatic effects were simply the aftermath of specific molecular injury, rather than the primary lesion itself.

The last paper was given by H. B. Newcombe who discussed the genetic effects, mentioning the widespread popular misunderstanding of these effects. He tried to draw a distinction between fact and speculation. One basic fact was that there was no threshold level below which no mutations would be produced; the number of mutations was proportional to the dose in a linear manner. Recent experiments in mice had also shown that mutation rate could be affected by dose rate. Another well-supported belief was that the great majority of these mutations were harmful. It was very difficult to assess levels of permissible exposure. Natural radiation gave us all a dose of three roentgens in a generation, and it was assumed though not proven that this was not harmful. It was essential to study the basic problems related to low dose effects over long periods, however difficult and unattractive this research might be.

CANADIAN PUBLIC HEALTH ASSOCIATION: 50th ANNIVERSARY MEETING

Six hundred public health personnel from across Canada attended the Jubilee Meeting of the Canadian Public Health Association in the Sheraton-Mount Royal Hotel, Montreal, June 1 to 3. Subjects covering a wide range of public health topics were discussed.

Senator Sarto Fournier, Mayor of Montreal, extended a warm welcome to the delegates on behalf of the city, and the Honourable Arthur Leclerc, M.D., Minister of Health for the Province of Quebec, did likewise for the province. The scientific portion of the meeting was liberally sprinkled with the traditional French Canadian hospitality of President Jules Gilbert; Dr. Cyrille Pomerleau, Président of La Société d'Hygiène et de Médecine Préventive de la Province de Québec; and the Montreal committee headed by health officer Adélard Groulx and his deputy, Gustave Charest. The city provided its customary excellent reception at the Chalet, and luncheon addresses were given by the Honourable Waldo Monteith, Minister of National Health and Welfare, on Monday, and by Dr. Halbert L. Dunn, Chief, National Office of Vital Statistics, Washington, on Tuesday. Mr. Monteith took the opportunity to describe control procedures currently carried out by his department to detect irradiation from various sources. He emphasized the importance of more research on the effect of irradiation on humans, particularly over a prolonged period of time. At the present time the effect of radioactive fallout does not appear to be significant. Dr. Margaret Nix, assistant professor, Department of Health and Social Medicine, McGill University, gave a very interesting address at the Jubilee Dinner, Tuesday evening. Her subject, "Five Million Reasons", reminded the audience that there are five million children in Canada who require our constant attention for proper health and development.

In reporting the Hospital and Diagnostic Services Program for the federal government, Dr. E. H. Lossing advised that there are now approximately eleven and one-half million residents in Canada covered under these programs. This represents 67% of the population. The federal government's participation in this program for the current fiscal year is expected to be $160,000,000. This represents one-half of the cost of the program. Provincial governments may begin their Hospital and Diagnostic Services Program any time during the year. Dr. Lossing predicted that outpatients' services will probably be extended as a means of relieving inpatient services.

Mr. Gordon L. Pickering, commissioner of hospitalization, Manitoba Hospital Services Plan, stated that the Manitoba program had been introduced with surprisingly few complications, considering that there was only about three months' planning before the program was instituted. Ninety-nine per cent of the population are covered in Manitoba. He said that social and economic factors and not medical factors contributed to lengthy hospital stays. This applies chiefly to old persons who need domiciliary or custodial care. In establishing a universal Hospital and Diagnostic Services Program, it would be better to provide improved housing for old people before embarking on such a program. He pointed out that there is a need for standardizing salaries of hospital personnel between provinces, in order to eliminate a good deal of travelling around by such personnel, who are constantly trying to better their financial positions. A master pension plan would also be helpful in this connection. Shortly after the Manitoba plan was introduced, a number of outpatients' services were added as benefits under the program, particularly minor surgical procedures. This has eliminated the admission to hospital of such cases.

Mr. John E. Sparks of the Research and Statistics Division, Department of National Health and Welfare, compared the national health bill in current dollars between 1953 and 1957, and indicated that hospital care had increased during that period 41% per capita, physicians' services 34%, prescribed drugs 43%, dental care 24%, and other services (including nursing, osteopathic, chiropractic, etc.) 48%. He pointed out that in 1959 it was estimated that 85% of the cost of providing hospital and diagnostic services in Canada would be financed by federal and provincial governments, whereas the remaining 15% would be paid by direct contributions by individuals. Before the federal health plan was introduced, individuals used to contribute 50% directly. Mr. Sparks stated that although hospital care and the cost of drugs had gone up more rapidly than other consumer goods and services in the same period, the cost of medical care had not. The cost of physicians' services has maintained a fairly constant relationship to the rising cost of other consumer goods and services. In 1953, 4.09% of personal consumer expenditures was for health care, and in 1957, 4.58%. In discussing this paper, Dr. Murray Acker of Regina pointed out that the Canadian Sickness Survey in 1950-1951 indicated that for every dollar spent on physicians' services 40 cents was also spent on prescribed drugs,

and approximately 60 cents per dollar for all drugs. Thirty cents is spent for dental care for every dollar on medical care. In describing voluntary medical care programs in Canada, Mr. Howard Shillington, executive director, Trans-Canada Medical Plans, estimated that approximately 53% of the people of Canada had some type of medical care coverage.

A notable occasion during the meeting was the award of an honorary Diploma in Public Health by the University of Montreal to Dr. R. D. Defries of Toronto for his outstanding contribution to public health.

The Resolutions Committee brought in a number of resolutions which were passed by the General Meeting on Wednesday morning. These resolutions included the following recommendations: that the federal and provincial departments of health give increased leadership in accident prevention; that studies of radiation, including medical radiation and atomic fallout, be continued and appropriate control programs set up; that a recruitment program for public health personnel be carried out among secondary-school children; that provincial governments be encouraged to establish enabling legislation to allow municipalities to fluoridate communal water supplies; that all milk used in public eating places and private and public institutions be pasteurized; that educational programs be carried out to inform the public of the relationship between cigarette smoking and lung cancer.

The nominating committee under the chairmanship of Dr. A. R. Foley of Quebec brought in the following nominations, which were unanimously approved by the meeting:

Honorary President: The Honourable R. A. Donahoe, Minister of Health, Province of Nova Scotia.

President: Dr. J. S. Robertson, Deputy Minister of Health, Province of Nova Scotia.

President-Elect: Dr. F. Burns Roth, Deputy Minister of Health, Province of Saskatchewan.

Vice-Presidents: Miss Phyllis Lyttle, Director of Nursing, Halifax; Dr. Owen H. Curtis, Deputy Minister of Health, Prince Edward Island; Dr. Murray Acker, Provincial Health Department, Saskatchewan.

Honorary Secretary: Dr. George Moss, Deputy Medical Officer of Health, City of Toronto.

Honorary Treasurer: Dr. W. Mosley, Professor of Public Health, School of Hygiene, University of Toronto.

Editor: Dr. R. D. Defries, Consultant, Connaught Medical Research Laboratories, University of Toronto.

CANADIAN PSYCHIATRIC ASSOCIATION

The eighth Annual Meeting of the Canadian Psychiatric Association, held at the Château Laurier, Ottawa, from June 4 to 6, 1959, erected a further milestone of great developmental significance in the growth of this active young group organism. Of the 552 members on the Association's list at the end of May, 132 psychiatrists were registered at the meeting, who together with 74 guests from other specialties and professions, participated in a full program of scientific, organizational, and social events. Their consensus as they said their farewells to return home was that the Association, if not yet fully mature, has certainly passed the epoch of puberty and is enjoying both the rewards and the pangs of an exceptionally vigorous adolescence, full of good promise for the future.

On the first day, while the outgoing Board of Directors was meeting at the University of Ottawa, the Association's newly formed Committee on Child Psychiatry held scientific and organizational sessions attended by over 80 members interested in this aspect of the specialty. In the morning Drs. Rosen, MacLeod, Asselstine and Tyhurst briefly described the development of psychiatric services for children in Toronto, Montreal, Winnipeg, and Vancouver, respectively. Dr. Denis Lazure then discussed recent developments in this field in the French-speaking community of Montreal. Later in the morning Drs. Rich and Frank shared with the group their experiences in the residential treatment of disturbed children, and the scientific session closed with an extremely stimulating paper by Dr. Nathan Epstein on his research investigations of urban families as total units, with particular attention to distortions of normal roles and relationships. In discussions later in the day, led by panels on problems of organization and of training standards, delegates expressed a wide diversity of viewpoints, agreed that while any monolithic dogmatism in these matters is impossible at present and probably undesirable in principle, there is urgent need for continuing communication concerning them in the supporting framework of group identity, and voted unanimously to recommend to the incoming Board of Directors that the *ad hoc* administration set up to arrange this meeting be replaced by a Standing Committee on Child Psychiatry. The day closed enjoyably with a banquet sponsored by Harterre House of Montreal.

On Friday morning, June 6, the first scientific session of the main meeting began with a panel presentation on "Techniques in brief psychotherapy", with Dr. W. Clifford M. Scott as chairman. Dr. Guild of Edmonton opened with a comprehensive statement of the structure and practical arrangements of brief therapy, its indications and contraindications, and the definition of its more or less limited goals. Dr. Watterson of Vancouver next outlined some of the complex processes which take place both within and between doctor and patient during therapy, thus supplying additional motivational evidence for Dr. Guild's formulations. Dr. V. Voyer then read a paper by Dr. Karl Stern, whose attendance was unhappily precluded on medical grounds, on the use of patients' dreams: with a wealth of vivid case material, Dr. Stern demonstrated that the "royal road to the unconscious" can be profitably travelled during the earliest phases of a short therapeutic process, no less than through the intricate course of a protracted analysis of traditional form. Dr. Roger Lemieux gave the final set contribution, on the important but too often neglected topic of the role of patients' families in the processes of treatment and recovery. An active discussion from the floor could have continued well beyond the imposed time limit.

All who heard it agreed that the Academic Lecture on "The treatment of criminal psychopathy", delivered by Prof. P. A. H. Baan of Utrecht, was a brilliant highlight of the meeting. Speaking from a wide background of training and experience in both law and

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psychiatry, Dr. Baan pointed out the glaring anomaly that in the average Western democracy, organized society spends more on the less than 1% of its population which exhibits compulsively repetitive delinquency, than on its entire educational system at all levels. He described fruitful experiments carried on by himself and his colleagues in the intensive institutional treatment of this group, involving team work among many professions and a high ratio of staff to patients. Noting that legal authorities have never been more ready to co-operate in any potentially useful approach, he urged psychiatrists collectively and individually to modify their hitherto negative and fatalistic attitudes toward these syndromes, of which he felt the constitutionally predetermined basis is ever less evident.

At luncheon, members and representative guests from the local professional community enjoyed a warmly humorous historical account of the conception, birth, and early years of the Association, given by its first President, Prof. R. O. Jones of Dalhousie, substituting at short notice for the out-going President, Prof. Cameron, who was absent from the meeting owing to illness. Such was the resulting euphoria that at the Annual Business Meeting which followed, members acquiesced without a murmur in a fee increase. Other items of business were handled with despatch under the skilful guidance of Dr. Lawson as Chairman, with credit due especially to the Secretary, Dr. C. A. Roberts, for efficient preparation of the agenda.

The social aspect of the Convention reached its apogee Friday evening with the President's Reception and the Annual Dinner and Dance, held at the Hull Armories. Meteorologically the discomfort index may have been unduly elevated, but the emotional and social climate was benign and balmy throughout. This mood was sustained in the after-dinner address of Alan Jarvis, Director of the National Gallery of Canada, who entered a spirited plea for more mutual attention between science and art in the interests of mental health, and vividly exemplified his point by the ease with which he held and swayed his audience.

The second scientific session on Saturday morning was devoted to research reports and clinical contributions, presided over by Drs. A. B. Stokes of Toronto and J. B. Boulanger of Montreal, respectively. Vancouver provided three contributions — from Dr. Richman on the research applications of electronic computers, Dr. Powles with a thoughtful examination of the concept of the therapeutic milieu, and Dr. Kenning of the Crease Clinic on the antidepressive efficacy of imipramine. Drs. Kral and Grad of Montreal reported the possibility of distinguishing senile psychoses from other conditions by physiological measurements of the responsivity of the adrenal cortex to minor stress. Prof. Bruce Sloane of Queen's outlined early results from very basic investigations of possible correlation of personality traits with susceptibility to atherosclerosis, on the basis of demonstrated differences between normal young adults showing extremes of blood cholesterol levels after periods of fasting. Dr. E. S. Goddard of London delivered a needed and impressive warning concerning the addictive properties of meprobamate, fortified by all too pertinent case material; and Dr. Donald Gunn of New Toronto demonstrated anew the potential of the provincial mental hospitals for wide-based clinical research, by his report of an impressive series of electroshock treatments carried out with complete safety and a minimum of patient apprehension by use of muscle relaxants. The morning closed on a stimulating exotic note, with Dr. R. H. Prince's fascinating report of both the lethal and the healing effects of witchcraft among the Yoruba natives of Nigeria, where curses and blessings, ritually delivered, retain undeniable validity. The last formal event of the Convention was the afternoon meeting of the newly elected Officers and Board of Directors for 1959-60, symbolizing the continuity of the organization and the prospect of another year of active growth.

Throughout the meetings, a representative group of exhibits by the pharmaceutical houses provided up-to-date information on chemotherapeutic advances for members and guests.

The Ladies' Committee, under Mrs. W. A. Blair's able direction, arranged a well-received program for delegates' wives, which included a tour of the capital in its early summer beauty, a luncheon at the Country Club, and a continental breakfast.

Officers for 1959-60 are: President, Dr. F. S. Lawson, Regina; Vice-President and President-Elect, Dr. J. G. Dewan, Toronto; Secretary, Dr. C. A. Roberts, Montreal; Treasurer, Dr. R. C. M. Hamilton, Ste-Anne-de-Bellevue; Honorary Counsel, Dr. K. G. Gray, Toronto.

All members contacted were firm in their resolve to be present at next year's meeting in Banff — and most felt that they would wish actively to promote the attendance of colleagues who were not with us in 1959.

PAUL A. CHRISTIE

WORLD CONFERENCE ON MEDICAL EDUCATION

The Second World Conference on Medical Education which is scheduled to be held in Chicago from August 29 to September 4 this year has now taken shape nicely. The conference is sponsored by the World Medical Association, the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Association of Universities, with President Eisenhower as Patron. It is expected that the President himself will address the opening plenary session on Monday, August 31.

The First World Conference on Medical Education was held in London in 1953, and the second conference will give medical educators an opportunity to examine progress made during the five-year interval in extending medical education and raising its standards. It is expected that between 1500 and 2000 persons from all over the world will attend the conference, at which there will be 125 speakers from about 50 countries. All business, including lectures, will be translated simultaneously into English, French and Spanish. Although not a member of W.M.A., Russia is expected to send a delegation to the conference and will have at least two speakers on the program, while Poland, another non-member, will also send representatives. The subjects of the four sectional sessions will be: (1) basic clinical training for all doctors; (2) advanced education for general and specialty practice; (3) the development of teachers and investigators; (4) continuing medical education.

LETTERS TO THE EDITOR

APATHETIC HYPERTHYROIDISM

To the Editor:

We would like to thank Drs. Lillington and Brownell for their interest and comments on our communication (81: 54, 1959). We may not have been sufficiently precise in our statements, since there appears to be some misunderstanding of our views. The term "classical hyperthyroidism" did not imply the presence of exophthalmos; it meant, as stated, the presence of those neuromuscular and cardiovascular abnormalities commonly associated with hyperthyroidism. In agreement with Plummer,[1] and with the generally accepted views of today,[2] we noted a fairly high incidence of exophthalmos in association with diffuse goitres with hyperthyroidism, and no exophthalmos in association with nodular goitre and hyperthyroidism. There would appear to be little disagreement concerning these associations.

We would disagree strongly, however, that we and others have misinterpreted Plummer's views. Drs. Lillington and Brownell have stated clearly the clinical picture which Plummer associated with toxic nodular goitre, and neither we nor others would disagree with the essential thesis that patients with this form of hyperthyroidism usually are older and do not have ocular manifestations of the disease. Plummer stated[1] that patients with toxic nodular goitre "may be divided into two *merging* [italics ours] groups: (1) a group in which the cardiac toxin predominates . . . ; (2) a group more closely approaching the picture of Graves's disease . . ." We are in entire agreement with this view of a spectrum of clinical pictures ranging from "classical hyperthyroidism", with or without exophthalmos, to "apathetic hyperthyroidism" in which cardiac manifestations are dominant. It is precisely this range which has led many observers to disagree with Plummer's concept that there are two distinct types of hyperthyroidism; they believe that grouping on the basis of exophthalmos clinically, and nodularity of goitre pathologically, is without any physiopathological basis other than that associated with the older age of those with nodular goitre. The future may very well bear out Plummer's thesis, but convincing evidence is not now at hand.

If patients with apathetic hyperthyroidism are excluded, we would disagree with the statement that "in toxic adenomatous goitre one or more nodules contain the hyperactive tissue and the remainder of the gland is suppressed". The correspondents have misinterpreted Dobyns[3] in this regard, since he clearly stated only that exophthalmos is associated with hyperactivity of paranodular tissue but not that non-exophthalmic cases always have suppression of paranodular tissue. None of our patients with "classical hyperthyroidism" and nodular goitre showed such suppression. If one now wishes to redefine "Graves's disease" and "Plummer's disease" along functional lines based on I^{131} distribution, it should be remembered that such a new classification may have little relation to the clinical picture.

We would like to restate the essential points of our paper:

(1) Hyperthyroidism may occur with primarily cardiovascular manifestations; this was recognized (many years before Plummer) by Charcot and by Chvostek.

(2) Hyperthyroidism may be due to localized hyperactivity of a nodule, with suppression of activity of the remainder of the gland; this has been shown clearly only since I^{131} became available.[4]

(3) We report our observations that these two phenomena are related.

Undoubtedly apathetic hyperthyroidism is being missed in some patients; thyroid scanning after I^{131} administration may give the clue to the correct diagnosis.

N. KALANT, M.D.,
D. L. WILANSKY, M.D.

Jewish General Hospital,
3755 St. Catherine Rd.,
Montreal, Quebec,
June 17, 1959.

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3. DOBYNS, B. M.: *Am. J. Med.*, **20**: 684, 1956.
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POLIOMYELITIS IN MANITOBA, 1958

To the Editor:

The report of the Winnipeg group (Wilt *et al.*, *Canad. M. A. J.*, 81: 1, 1959) on the efficacy of the Salk poliomyelitis vaccine and the virological findings is of great interest. The vaccine has continued to be of interest since the first trial was reported by Francis. The dramatic drop in Canada in the incidence of poliomyelitis from an all-time high of 8734 cases in 1953 to 253 cases in 1958 might be taken as evidence of the efficacy of the vaccine. To attribute this drop entirely to the effects of the vaccination program must be accepted with caution. The complex factors which determine the wide annual variations in this unpredictable disease are largely unknown. It is reports of this kind which help to establish the effectiveness of the vaccine.

The authors have gone to considerable effort to determine the approximate percentage of the population immunized, as indicated in Table III and Fig. 4. From these estimated figures the following table of rates of paralytic poliomyelitis in the not fully vaccinated and the fully vaccinated groups was prepared.

PARALYTIC POLIOMYELITIS, MANITOBA, 1958

Age group	*Rate per 100,000*	
	Not fully vaccinated	*Three doses of vaccine*
0 - 4	74	10
5 - 9	36	4
10 - 14	29	2
15 - 19	8	0
20 - 39	21	3
40+	1	0

It should be noted that in some instances these rates are based upon very small numbers of cases. However, if the estimated figures of the percentage vaccinated are representative of the actual state of vaccination, they suggest a high degree of effectiveness of some-

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thing in the order of an 80% reduction for the Salk vaccine used in this instance.

The small percentage of the 20-39 year age group estimated to have been vaccinated is a matter of concern. A more concentrated effort should be made to protect this age group because of the increased severity of the disease as noted by the authors. Poliomyelitis is becoming a disease of adults.

School of Hygiene,
University of Toronto,
Toronto 5, Ont.,
June 22, 1959.

MILTON H. BROWN, M.D.,
Professor of Public Health
and Preventive Medicine.

FLUORIDATION

To the Editor:

Professor Mather, referring to the controversy over the fluoridation of the communal water supplies, states (*Canad. M. A. J.*, 80: 918, 1959) that "one should be clear that this is a political controversy". He states this in such a manner as to indicate that once the profession has made up its mind as to what is good for the people—there should be no controversy. The unfortunate fact is that the profession has never realized the political implication of its stand in this matter. This is indeed a controversy between socialized medicine and private medicine, even though the socialized medicine be disguised by the name of public health.

A clear distinction must be drawn between the rights and privileges of the individual and society so that we may understand what may be tolerated in public health and what is indeed socialization of medicine under another name. I have attempted to outline this distinction in a previous letter (*Canad. M. A. J.*, 78: 64, 1958). Briefly, again, in regard to the individual person, the distinction is:

1. If a person is ill and his illness does not constitute a menace to society—he should determine how and if he will be treated, although society may offer its aid. This is private medicine.

2. If an individual is ill with such a disease as constitutes a menace to society, society may deal with him in such a way as to remove the menace. This is public health.

3. If an individual is ill with such a disease as constitutes no menace to society and society force him to treat that illness—this is socialized medicine, for it is a prostitution of private medicine practised not for the person but for society. This we must avoid and to this category belongs fluoridation of the water supply. The evil of socialization is not state control of the profession but state control of the patient.

We have, of ourselves, no right to practise medicine. It is a privilege granted by each one of our patients. Surely it is up to us who enjoy this privilege to see that our patients are kept free to grant it.

Space does not permit of the refutation of the contention that fluoridation is no different from chlorination, vaccination, etc. Suffice it to say at the moment that a cursory examination of the principles involved will soon show that there is no true analogy.

C. P. HARRISON, M.D.,

604 Columbia St.,
New Westminster, B.C.,
June 13, 1959.

BISACODYL (DULCOLAX) AS A POSTOPERATIVE LAXATIVE

To the Editor:

I recently read the article by Drs. Lavoie and Murat on bisacodyl (Dulcolax) in the May 1 issue of your Journal (80: 719, 1959) and would like to make a couple of comments for the benefit of practising physicians and surgeons who may be using or wish to use this laxative.

The first point that should be mentioned is that although Drs. Lavoie and Murat state that bisacodyl is not toxic whether given in massive doses or after prolonged use and also that no major side reactions were encountered with either method of administration, they have not mentioned the one side effect which does occur from administration of this laxative. This is abdominal cramps. I recently had personal experience with this laxative and on each of three occasions on which the tablets were taken, each tablet was followed with very severe abdominal cramps. This was also noted in a female patient postoperatively when it was used in suppository form and also by a graduate nurse on the ward who took one tablet orally. This is sufficiently important to mention, as the abdominal pains may be erroneously attributed to postoperative complications rather than to the medication or vice versa.

The second point is that I would like to recommend the suppository as a means for obtaining stool specimens for laboratory examination, as it is not always possible for the patient to defæcate at the opportune time for the laboratory technicians. Specimens can usually be obtained within 15 to 30 minutes following the insertion of a bisacodyl suppository.

Manitoba Clinic,
790 Sherbrook St.,
Winnipeg 2, Man.,
June 2, 1959.

C. B. SCHOEMPERLEN, M.D.

To the Editor:

In our article we did not mention abdominal cramps as a side effect of the administration of bisacodyl (Dulcolax) postoperatively, because we did not have any complaint of that kind. In two or three instances, patients mentioned slight discomfort in the abdomen.

However, we have sometimes encountered severe abdominal cramps in normal subjects given bisacodyl (i.e., not after abdominal surgery), usually when the tablet form was used. There is an explanation for this; after abdominal surgery, there is always a degree of intestinal paralysis, and the bowels do not react to bisacodyl as violently as in a normal person and do not contract completely.

We agree with Dr. Schoemperlen, and we thank him for his suggestion that the suppository form of bisacodyl be used when obtaining stool specimens for laboratory examination.

JULES LAVOIE, M.D., F.I.C.S.

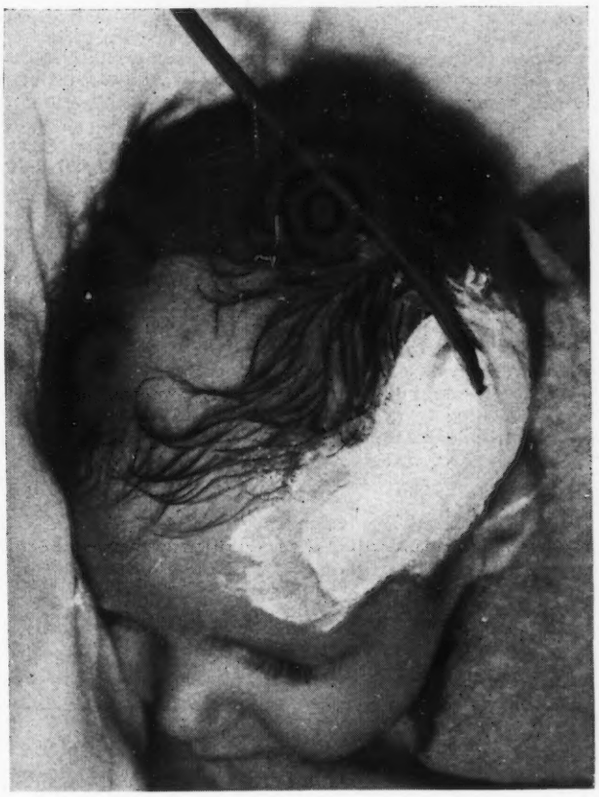
St-Georges de Beauce, P.Q.,
June 8, 1959.

SCALP VEIN INFUSION

To the Editor:

I was most interested in Dr. Zaidi's description of a method of protecting the needle of a scalp vein infusion in infants, in your issue of April 15, 1959, in order to prevent the extravasation of fluid into the subcutaneous tissues.

This brought to my mind another useful device for immobilizing the scalp vein needle. The method, to my knowledge, was first introduced at Booth Hall Children's Hospital and Pendlebury Children's Hospital, in Manchester, England, about 1950.



The appliance was dubbed the "tombstone" by the residents because of its appearance. Briefly, it consists of 2-3 plaster-of-Paris strips measuring ½" x 2", moistened once and then placed beneath the hub of the needle (already in the scalp vein) in such a manner as to form a plaster bed, thus immobilizing the needle in the ideal position for the free flow of the intravenous fluid. This is then reinforced with further plaster strips placed across the scalp vein needle and plaster bed.

Needles have been maintained in position by this method for 48 hours or longer. Nursing staff and residents have testified to the effectiveness of the device, as the infant can be changed or fed out of his crib, or even allowed to roam around the crib, without disturbing the intravenous infusion.

The accompanying photograph illustrates this method.

2011 Victoria Park Ave.,
Scarborough, Ont.,
May 23, 1959.

NATHAN SHER, M.D.,
M.R.C.P.(Edin.)

"CHINESE MEDICINE MARCHES ON"

To the Editor:

The paragraph on page 890 of the June 1 issue entitled "Chinese Medicine Marches On" is a sad commentary on what happens to a good medical journal when it comes under the control of a Communist government. In my nine years in China, I never came across any of the cures claimed by this article, and many of my patients came after having used up all their money for the traditional treatment of their diseases.

Contributors to the *Chinese Medical Journal* were just as aware as present writers of the claims of ancient Chinese medicine, and there were frequent articles describing examination of old Chinese remedies. However, they did not agree with the extravagant claims made in the article which you have quoted.

17 Downing St.,
Brantford, Ont.,
June 21, 1959.

R. HAYWARD, B.A., M.D.

VITAMIN E IN CHRONIC POLIOMYELITIS

To the Editor:

I would like to record some clinical observations which I have made on the beneficial effects of vitamin E therapy in chronic poliomyelitis patients.

It is a well-known fact that numerous and varied symptoms arise in chronic poliomyelitis patients with extensive residual paralysis. Some of the more distressing are muscle cramps, tingling sensations and a feeling of coldness in the affected limbs. Having had previous success in treating aged persons suffering from nocturnal muscle cramps with vitamin E, the writer prescribed vitamin E in the form of the succinate for eight chronic poliomyelitis patients complaining of the above symptoms and noted satisfactory results in most cases.

Case 1: D.A., a male aged 28 with complete paralysis of the extremities of four years' duration, complained of muscle cramps and painful ankle swelling. He was given 1600 units of vitamin E per day for one month, in which time the cramps cleared and the ankle swelling lessened.

Case 2: L.S., female, aged 19, developed poliomyelitis in 1953 with extensive paralysis and wasting of the left leg. She complained of crampy pains and a feeling of coldness in the leg. Eight hundred units of vitamin E succinate per day was given for four weeks. The crampy pains cleared and a generalized feeling of warmth to the leg was noted both subjectively and objectively.

Case 3: A.G., female, aged 42, developed poliomyelitis in 1950 with complete paralysis of the right leg and partial paralysis of the left. She complained of increasing crampy pains, tingling sensations and numbness in the right leg. Because her condition did not respond to conventional therapy, she was given 800 units of vitamin E per day for three weeks, at which time her symptoms cleared. After 10 days off the drug the symptoms returned.

Both Cases 2 and 3 are symptom-free on a sustaining dose of 400 units a day.

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Cases 4 and 5: Two women with almost complete paralysis and vital capacities of 400 and 500 c.c., necessitating respiratory assistance eight hours each day, complained of crampy pains and were subject to cyanotic pallor when fatigued. One was given 1600 units a day, the other 800 units for one month, and the pain cleared while the cyanotic pallor disappeared. Discontinuing the drug led to return of the cyanosis.

The author also found vitamin E of advantage in its effect on menstruation. Two women developed amenorrhœa following the onset of poliomyelitis, one for 14 months and one for nine months. Neither case responded to œstrogen therapy. After receiving 400 units of vitamin E for one month, both patients commenced menstruating and remained regular after the drug was discontinued. Three women with marked irregularity following their poliomyelitis infection became regular and remained so after one month on vitamin E therapy.

The writer is convinced that vitamin E is of value in the treatment of chronic poliomyelitis patients with symptoms of peripheral vascular origin. He feels that the drug should be tried on a larger series of patients in order to estimate its true worth.

W. H. JACQUES, M.D.,
Medical Director.

Riverdale Isolation Hospital,
St. Matthews Road,
Toronto 8, Ont.,
June 15, 1959.

The writer on behalf of his patients and himself wishes to thank Webber Pharmaceuticals Limited, Toronto, Canada, for the generous supply of vitamin E succinate used in the treatment of symptoms so commonly found in chronic poliomyelitis cases.

PUBLIC HEALTH

SURVEILLANCE REPORTS OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

Paralytic Poliomyelitis

Canada

Twenty-three cases of paralytic poliomyelitis have been reported up to May 30, 1959. Nine of these cases occurred early in the year among Eskimos in the north-eastern Arctic. In 1958, up to this date, 23 cases were reported.

United States

In the first 20 weeks of 1959, 329 cases of paralytic poliomyelitis were reported, compared with 175 for the same period last year.

Influenza

During March and April 1959, over 1600 cases of influenza were reported among personnel in the Canadian Army. Most of the cases reported from the Maritimes and the Province of Quebec occurred towards the end of March and the beginning of April. The Ontario cases occurred from the middle of March to the third week in April. In Manitoba, most of the cases occurred from the second week in April onwards.

Two further outbreaks were reported from Alberta for the month of April. In Drayton Valley there were about 500 cases affecting mostly children in schools, and in the Vulcan and High River district about 250 cases were reported.

An outbreak of influenza-like illness has been reported from Fort Good Hope, Northwest Territories, affecting 95% of the population.

United States

In the winter-spring influenza season, there were several causative agents, the Type B being the predominant virus in most parts of the country. Other isolations were of Type A, Type A1 and A2. During May, only a few reports of new outbreaks were received. Most of the cases reported this season occurred among children of school age, and epidemic influenza among adults has been conspicuous by its absence. The influenza-pneumonia deaths reported from 108 United States cities stand at a level normal for the season.

Streptococcal Sore Throat

About 100 cases of streptococcal sore throat have been reported from the Claresholm district in Alberta, occurring mostly among school children and young adults.

In Canada to May 16, 1959, 11,493 cases of scarlet fever and streptococcal sore throat were reported, against 4905 for the same period in 1958. The five-year median, 1954-1958, for the corresponding period was 4836.

Food Poisoning

An outbreak of food poisoning was reported from an R.C.A.F. station in Ontario. Eighty-five persons reported at the morning sick parade complaining of diarrhœa. The previous evening about 300 to 400 people consumed a meal of meat stew and gravy and custard pie. The symptoms started around 3 o'clock in the morning. Samples of the food eaten were not available for examination. All the stools examined were negative.

Gastroenteritis

An outbreak of gastroenteritis has been reported from Cambridge Bay, Northwest Territories, affecting Eskimos and whites. Two babies died. A medical officer was flown in to investigate and treat the condition.

Shigellosis

The Ste-Justine Hospital, Montreal, reports a case of shigellosis in a three-year-old child. His home is in Algoma County, Ontario.

Trichinosis

Two cases of trichinosis were reported in the province of Quebec.

Giardia Lamblia Infestation

Two cases of giardiasis have been reported from 100 Mile House, British Columbia.

Infectious Hepatitis

As a continuation of an outbreak previously reported, 14 more cases of infectious hepatitis were reported in the Taber and Coaldale area in Alberta.

In Canada from January 1 to May 16, 1959, 2417 cases of infectious hepatitis were reported, compared with 1334 cases for the same period in 1958 and 1399 for the corresponding five-year median 1954-1958. There is an appreciable increase in the incidence of infectious hepatitis in Ontario, Manitoba and British Columbia.

Psittacosis

One case of psittacosis has been reported from Edmonton, Alberta. The patient was a young woman on the staff of the veterinary laboratory of the Provincial Department of Agriculture. She developed an influenza-like illness two weeks after handling a dead budgerigar. Serological examination confirmed the diagnosis. Psittacosis was identified as the cause of the bird's death.

June 6, 1959. Epidemiology Division, Department of National Health and Welfare, Ottawa.

SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA*
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

	Week ended (1959)				Cumulative total since beginning of year	
	May 2	May 9	May 16	May 23	1959	1958
Brucellosis (Undulant fever) (044)	5	6	—	1	36	26
Diarrhœa of the newborn, epidemic (764)	2	—	1	2	31	**
Diphtheria (055)	—	—	—	1	14	23
Dysentery:	10	10	—	—		
(a) Amœbic (046)	—	—	—	—	2	4
(b) Bacillary (045)	10	10	9	12	324	180
(c) Unspecified (048)	—	—	7	—	18	—
Encephalitis, infectious (082.0)	3	1	1	1	10	8
Food poisoning:	12	8				
(a) Staphylococcus intoxication (049.0)	—	—	—	—	5	—
(b) Salmonella infections (042.1)	12	8	4	14	141	196
(c) Unspecified (049.2)	—	—	—	—	40	93
Hepatitis, infectious			—	—		
(including serum hepatitis) (092, N998.5)	142	83	69	47	2,464	1,448
Meningitis, viral or aseptic (080.2, 082.1)	—	—	3	—	26	3
Meningococcal infections (057)	9	3	1	3	93	126
Pemphigus neonatorum (Impetigo of the newborn) (766)	—	—	—	—	1	**
Pertussis (Whooping cough) (056)	106	114	114	180	2,459	2,423
Poliomyelitis, paralytic (080.0, 080.1)	—	—	2	1	13	15
Scarlet fever and Streptococcal sore throat (050, 051)	646	548	516	502	12,007	5,114
Tuberculosis:	117	99				
(a) Pulmonary (001, 002)	84	81	116	71	1,859	2,453
(b) Other and unspecified (003-019)	33	18	34	17	575	771
Typhoid and Paratyphoid fever (040, 041)	20	35	11	22	348	115
Venereal diseases:	322	282				
(a) Gonorrhœa (030-035)	277	241	263	235	5,310	5,646
(b) Syphilis (020-029)	45	41	48	37	785	796
(c) Other† (036-039)	—	—	—	—	3	2

*Excluding Northwest Territories. Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.
†Including chancroid, granuloma inguinale and lymphogranuloma venereum.
**Not reportable.

DEPARTMENT OF NATIONAL HEALTH AND WELFARE
PARALYTIC POLIOMYELITIS IN CANADA—WEEKLY RETURN*
WEEK ENDING MAY 9, 1959

	Reported cases					Deaths	
	1959			1958		1959	1958
	This week	Last week	To this date	This week	To this date	To this date	To this date
Canada			18		11	5	1
Newfoundland							
Prince Edward Island							
Nova Scotia							
New Brunswick							
Quebec			3				
Ontario			3		3	1	1
Manitoba			1		1		
Saskatchewan							
Alberta			2		5		
British Columbia					2		
Yukon							
Northwest Territories			9			4	

WEEK ENDING MAY 16, 1959

Canada	2		20	1	15	5	2
Newfoundland							
Prince Edward Island							
Nova Scotia							
New Brunswick							1
Quebec	2		5		3		
Ontario			3		3	1	1
Manitoba			1	1	2		
Saskatchewan							
Alberta			2		5		
British Columbia					2		
Yukon							
Northwest Territories			9			4	

*These figures are based on weekly telegraphic reports by the provinces.

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OBITUARIES

DR. M. CYNBERG, 66, died on May 18 in the Senneville Veterans' Hospital, Senneville, Quebec. A native of Poland, he received his medical degree from the Warsaw Medical School in 1923 and practised internal medicine in Zamosc, Poland, until 1939. In World War II Dr. Cynberg served with the British Eighth Army under Polish command. He came to Canada in 1948 and joined the staff of the Senneville Veterans' Hospital.

Dr. Cynberg is survived by his widow, a daughter and a son, Dr. David Cynberg.

DR FERDINAND DEROME, ancien médecin-chef du district Saint-Jacques de Montréal, est décédé le 24 juin. Il avait été reçu à l'Université de Montréal et détenait un doctorat en hygiène de l'Université de Toronto.

DR. C. W. HENDERS, 73, died at the Toronto General Hospital on April 8. He had been ill since Easter. He was born in Mount Forest, Ont., and graduated in medicine from the University of Toronto in 1911. For seven years after graduation he practised in rural Ontario and in southern Alberta before returning to Toronto in 1925.

Dr. Henders is survived by his widow, a son and a daughter.

DR. LOUIS-DE-GONZAGUE JOUBERT died on June 17. He was Chief of Otolaryngology at Hôtel-Dieu Hospital of Montreal and associate professor at the University of Montreal. A graduate of Laval University, Dr. Joubert served in the C.A.M.C. during the First World War, after which he did postgraduate work in Paris. In his 40 years of practice he was also on the staff of Queen Mary Veterans' Hospital and of the Canadian National Institute for the Blind, and acted as consultant at the Verdun General Hospital.

He is survived by his widow and several children, among whom Dr. Jacques Joubert is in practice at Buckingham and Miss Marthe Joubert is a graduate nurse from Hôtel-Dieu.

DR M.-HYACINTHE LEBEL de Montréal est mort le 17 juin. Né à Cacouna, il avait été reçu en médecine à l'Université de Montréal en 1904 et avait poursuivi ses études à Paris. Le docteur Lebel faisait partie du personnel médical de l'Hôtel-Dieu et de l'hôpital général de Verdun et était professeur agrégé à la faculté de médecine de l'Université de Montréal. Il appartenait à plusieurs sociétés médicales (dont l'A.M.C., depuis 1929). Parmi les nombreux membres de sa famille qui lui survivent se trouvent ses fils les docteurs Léon et Jacques Lebel, tous deux de Montréal.

DR. D. N. McLEOD, 33, who graduated in medicine in Toronto in 1948, died on May 5, 1959, at Tucson, Arizona. He was the son of Dr. and Mrs. N. D. McLeod of Tillsonburg, Ontario. While an undergraduate at the University of Toronto, it was known by a few of his friends only that he had severe bilateral bronchiectasis. In spite of this handicap, he completed his medical course and two years' internship at the Toronto General Hospital before moving to Tucson, Arizona, in 1951. Here, over a short period of eight years, he gained the respect of the whole medical society, built a clinic building and established the largest general practice in Tucson. Although his practice was large, he gave considerate and kind care to all. From the standpoint of his respiratory disease, his health prospered. Unfortunately, however, he developed an aplastic anæmia which ultimately led to his death. He worked almost to the last, although he realized his health was failing. He died after a short vacation in Mexico.

Dr. McLeod is survived by his widow and two children. He will always be remembered for his courage and steadfastness in the face of disabilities which would have discouraged most of us. E.G.C.

DR. WILLIS MERRITT, 84, died on May 4 at the Holy Cross Hospital, Calgary. Born in Smithville, Ont., he was educated at the University of Toronto, where he graduated in 1905. He was also a postgraduate of the Johns Hopkins University, Baltimore. For 49 years Dr. Merritt lived in Calgary, and he practised there until his retirement. In 1948 he was made a senior member of the Canadian Medical Association.

He is survived by one son.

DR. P. O'KELLY, 56, died at St. Clare's Mercy Hospital, St. John's, Newfoundland, on May 13 after a short illness. A native of Cork, Ireland, he received his medical education at the National University of Ireland, University College, Cork, and graduated in 1925. In 1927 he came to Canada and started to practise in Avondale, Newfoundland.

Dr. O'Kelly is survived by his widow and a daughter.

DR. GRANTLY DICK-READ

A somewhat controversial figure in obstetrics died last month (June 11) in Norfolk, England, at the age of 69. Dr. Grantly Dick-Read, whose name is particularly connected with the expression "natural childbirth", received his medical education in the University of Cambridge and the London Hospital, and then spent several years in the British Army. He later became a general practitioner in Woking, a town near London, and then specialized in obstetrics in London. He was convinced that the pain of labour was due to a distortion of a physiological process, which should really be free from pain. His teaching that fear causes tension and tension causes pain was put forth in his publication *Natural Childbirth* in 1933 and this theory, somewhat difficult to prove scientifically, was proclaimed enthusiastically by himself and a growing number of followers. Although some of his beliefs were never wholeheartedly accepted by his colleagues, there is little doubt that he had a profound influence on the attitude to labour as a physiological act, an influence which extended to such countries as the Soviet Union, France and the United States. His last appearance in Canada was last year at the International Congress of Obstetrics when he read a paper on his favourite topic.

ABSTRACTS *from current literature*

MEDICINE

Sarcoidosis With Vertebral Involvement.

T. RODMAN, E. E. FUNDERBURK, JR., AND R. M. MYERSON: *Ann. Int. Med.*, 50: 213, 1959.

Although sarcoidosis is characterized by its capacity to affect many different systems, including the skeleton, vertebral lesions are rarely mentioned. The patient described in the present report appears to be the first in whom the histological diagnosis of vertebral sarcoidosis was made ante mortem. Apart from involvement of pulmonary lymph nodes, lesions of a "lytic" character were noted roentgenographically in the 11th and 12th thoracic vertebræ. Biopsy of lymph nodes revealed changes compatible with sarcoidosis. The patient had an inversion of the albumin:globulin ratio, and tuberculin and fungus skin tests were negative.

Because of the roentgenographic evidence of extension of the vertebral lesions, a spinal fusion was carried out. Biopsy revealed non-caseating granuloma. Special cultures for acid-fast bacilli and cultures for tubercle bacilli, fungi, and pyogenic organisms were negative.

It is suggested that sarcoidosis should be taken into consideration in differential diagnosis of destructive vertebral lesions, and that this possibility should be investigated in patients known to suffer from sarcoidosis.

S. J. SHANE

Acute Pericarditis as Initial Manifestation of Infectious Mononucleosis.

C. C. GARDNER, JR.: *Am. J. M. Sc.*, 237: 352, 1959.

An acute pericarditis was followed 10 days later by clinical infectious mononucleosis. The pericarditis was characteristically of acute idiopathic type. Acute pericarditis is considered by the author and by others to be one of the varied manifestations of infectious mononucleosis, and this variety of pericarditis should not, strictly speaking, be included in the idiopathic category. With the increasing precision in diagnosis of virus diseases by serological and isolation methods, it seems likely that more and more cases of acute benign pericarditis will be separated from the idiopathic group.

S. J. SHANE

Detection of Intrahepatic Metastases by Blind Needle Liver Biopsy.

A. D. PARETS: *Am. J. M. Sc.*, 237: 335, 1959.

Blind needle liver biopsy was performed in 113 patients for detection of intrahepatic neoplasm. Metastatic carcinoma was found in 72 patients (64%), primary hepatic carcinoma in four patients. Among the 72 patients with intrahepatic metastases, two serious complications developed after needle biopsy. One patient bled into the peritoneal cavity and required operation for control of hæmorrhage; another developed mild peritonitis secondary to perforation of an abdominal viscus. Both patients recovered uneventfully.

Blind needle liver biopsy is not entirely free from risk, but this can be minimized by careful selection of patients, adequate pre-biopsy studies, adherence to contraindications and skilful technique. Taking into consideration the fact that not all deaths due to needle liver biopsy are reported, the author believes that current data do not support the contention that liver biopsy performed in the presence of suspected liver metastases is significantly more hazardous than needle biopsy carried out for other proper indications.

S. J. SHANE

Pulmonary Cystic Disease: Observations in Cases Treated by Exploratory Thoracotomy.

M. H. JORESS: *Dis. Chest*, 35: 256, 1959.

Respiratory embarrassment resulting from spontaneous pneumothorax is common in cystic disease of the lungs. The patient may have numerous cysts, even bilaterally, yet he will have little if any respiratory distress unless a large cyst compresses normally functioning lung, in which case dyspnœa is an outstanding symptom. Roentgenological abnormalities complicating cystic disease can readily obscure the underlying cystic condition, noted in over half the cases described in this paper. Spontaneous pneumothorax is a common manifestation of cystic disease and it may recur frequently. Diffuse unilateral or bilateral emphysema as an accompaniment of localized cystic disease was not found in this series of cases. Although generally not considered in diagnosis, infection and hæmorrhage occur in cystic disease, and the basic disease can readily be missed. Exploratory thoracotomy is proving a realistic and fruitful approach to the problem of spontaneous pneumothorax, as well as the arrest of continuing dyspnœa associated with cyst formation resulting from compression of normal lung parenchyma.

S. J. SHANE

Serum Hepatitis from Whole Blood: Incidence and Relation to Source of Blood.

C. M. KUNIN: *Am. J. M. Sc.*, 237: 293, 1959.

Data on the incidence of homologous serum hepatitis at two veterans' hospitals during a six-year period are presented. The relation of a single commercial source of blood to an increased incidence of serum hepatitis during years in which it was used is outlined. This relation implies either inadequate screening methods on the part of this bank or the procurement of blood from a population with an unusually high incidence of carriers, or both. It is suggested that the use of blood from certain banks or other sources should be curtailed until their procedures are reviewed.

S. J. SHANE

Transaminases in Serum and Liver Correlated with Liver Cell Necrosis in Needle Aspiration Biopsies.

S. ZELMAN, C. C. WANG AND I. APPELHANZ: *Am. J. M. Sc.*, 237: 323, 1959.

During 143 aspiration biopsies of liver on 108 patients, serum glutamic-oxaloacetic transaminase was determined 130 times and serum glutamic-pyruvic transaminase 50 times. Extent of necrosis of liver cells as estimated in biopsy specimens correlated excellently with rise in serum activity of either transaminase. Degree of necrosis of liver cells was inversely related to 25 tissue glutamic-oxaloacetic and 13 tissue glutamic-pyruvic transaminase activity values determined in companion liver biopsy specimens.

The trauma of needle biopsy of the liver failed to affect the serum glutamic-oxaloacetic transaminase activity in 20 patients re-examined the following day.

S. J. SHANE

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SURGERY

Penetrating Wounds of the Chest.
R. E. NETTERVILLE AND R. MARTIN, JR.: *Dis. Chest*, 35: 62, 1959.

The authors report their findings in 101 cases of penetrating and perforating wounds of the chest seen in private practice since 1952. They discuss the common factors in the treatment of the acute phases and of the complications of these conditions. They believe that aspiration of the hæmothorax is preferable to catheter drainage. In traumatic pneumothorax, the lung can sometimes be re-expanded by aspiration. However, in cases of persistent air leak, as indicated by increase of pneumothorax, progression of subcutaneous emphysema or tension pneumothorax, catheter drainage should be used.

Of the 101 cases treated, 36 did not require surgical intervention and could be managed with local treatment to the wound, antibiotics, and antitetanus immunization. Fifty-one cases required drainage by thoracentesis. Catheter drainage was utilized in 17 cases. Eight patients required thoracotomy, and among these there were three decortications. Laparotomy was required in eight patients. S. J. SHANE

Mitral Valve Surgery: Transventricular Valvuloplasty and Use of Ivalon Sponge Pack for Mitral Insufficiency.
W. S. CONKLIN, G. L. MAURICE AND S. F. BERQUIST: *Dis. Chest*, 35: 291, 1959.

The authors review some of the techniques applicable to mitral valve surgery and emphasize the need for flexibility of approach and improvement in methods. Some of the techniques reported here are not original with the authors but derive from reports previously published by other cardiac surgeons.

Surgical experiences over a one-year period in 64 cases of mitral valvular disease are presented. Results, while favourable, are early and evaluation therefore must be guarded. Valvular stenosis resisting finger fracture has responded uniformly well to transventricular use of the Brock dilator. Murmurs have been greatly reduced or eliminated. Patients with mitral regurgitation complicating other valvular disease have had their regurgitation reduced or eliminated with use of an intrapericardial ivalon sponge pack. Gratifying improvement has been seen in two of three patients with severe "isolated" mitral insufficiency. In such cases, the pack is placed against the posterior aspect of the heart in the axis of the A-V sulcus, and held in place, without suturing, by the pressure of the closed pericardial sac. This pushes the left ventricular wall forward, so that the septal leaflet flaps against it, thus decreasing the degree of regurgitation. S. J. SHANE

Acute Varicocele: A Vascular Clue to Renal Tumour.
J. S. SPITTEL, JR., J. H. DEWEERD AND R. M. SHICK: *Proc. Staff Meet. Mayo Clin.*, 34: 134, 1959.

It is emphasized that acute varicocele is a finding worthy of note and should alert the physician to the possibility of a tumour in the corresponding renal zone. Although usually a late sign in cases of hypernephroma, it may be the initial manifestation of this tumour. Characteristically the acute varicocele associated with a renal tumour disappears when the latter is removed. Three cases of this combination of findings are described. S. J. SHANE

Surgical Management of Tic Douloureux.
E. S. GURDJIAN, J. E. WEBSTER AND D. W. LINDNER: *Surgery*, 45: 264, 1959.

This paper deals with 391 operations performed for tic douloureux. The diagnosis of the condition is discussed. The first attacks of pain should be treated conservatively. For repeated bouts, the authors prefer decompression of the trigeminal ganglion and find that it relieves 75-80% of patients. The remainder are candidates for incomplete section of the sensory root behind the ganglion (as originally advocated by Frazier in 1925).

The techniques for decompression and for root section are described through a temporal approach. Subtotal section of the root is preferable to complete section in order to prevent corneal ulceration by sparing the ophthalmic fibres. A few cases had section of the sensory root of the trigeminal nerve in the posterior fossa, medullary tractotomy or avulsion of the fifth nerves on the face.

Although the authors state that decompression of the sensory root has been a satisfactory first step in management in 83% of patients, their figures do not seem to support this. They have performed 276 rhizotomies (division of nerve roots) and only 62 decompressions. T. A. MCLENNAN

Long-term Effects of Splenectomy *(in German)*.
H. BEGEMANN AND W. GEHLE: *Deutsche med. Wchnschr.*, 84: 449, 1959.

A study was undertaken of 310 previously apparently healthy persons who had undergone splenectomy because of traumatic rupture of the spleen. Of the patients, 70 died postoperatively, mainly because of severe blood loss or the nature of the trauma. The average time since splenectomy in the surviving patients was 8½ years, with a range of 6 months to 36 years; the ages at operation ranged from 4 years to 67 years, by healthy persons, especially the young.

The authors report in detail findings regarding tendency to infection, circulatory disturbances, status of sexual function and fertility, blood picture and other miscellaneous matters. They conclude that there is no evidence that splenectomy is in itself responsible for any serious disorder or disability; it is tolerated well by healthy persons, especially the young.

W. GROBIN

Surgical Management of Hodgkin's Disease.
D. P. SLAUGHTER, S. G. ECONOMOU AND H. W. SOUTHWICK: *Ann. Surg.*, 148: 705, 1958.

A group of 18 patients with localized Hodgkin's disease were treated over five years ago by regional node dissection, and ten of them had local postoperative irradiation. Eleven are living five to 13 years later and show no signs of recurrence.

It is suggested that Hodgkin's disease may have a temporary localized phase in which it may be eliminated by aggressive measures. That surgery offers as good results as irradiation without the likelihood of progressive effects is argued. The commonly held belief that the diagnosis of Hodgkin's disease means a certain early death is untrue. It is worth while to attack the disease actively, if only one lymphnode-bearing area is affected, the chest radiograph is negative, the spleen is not enlarged, and there is no fever, eosinophilia, splenomegaly or pruritus. BURNS PLEWES

THERAPEUTICS

Ataractic Therapy in Tuberculous Psychiatric Patients.
R. A. FISHER AND E. TELLER: *Dis. Chest,* 35: 134, 1959.

Various combinations of tranquillizing drugs were given to four groups of neuropsychiatric tuberculous patients. Alseroxylon, reserpine, chlorpromazine and a combination of the latter two drugs were used. The results indicated that ataractics appear to be of value as adjuvants in the management and treatment of psychiatric tuberculous patients. Most improved sufficiently to permit psychiatric discharge, and there was a definite beneficial effect of the tranquillizing drugs upon the course of the tuberculous condition. The combination of chlorpromazine and a reserpine preparation produced the beneficial effect most rapidly. Serious side reactions were not encountered. The ataractics used had no direct therapeutic effect on the tuberculosis. S. J. SHANE

Reversal of Cardiotoxic Effects of Procaine Amide by Molar Sodium Lactate.
S. BELLET *et al.*: *Am. J. M. Sc.,* 237: 177, 1959.

The therapeutic effect of molar sodium lactate during procaine amide toxicity was studied in two groups of dogs, one given a continuous procaine amide infusion until death and the other similarly treated but in which the effects of molar sodium lactate were studied at various stages of procaine amide toxicity. ECG abnormalities and hypotension due to procaine amide toxicity were consistently and markedly improved by use of molar sodium lactate, which was effective at a more advanced stage than with quinidine toxicity.

Infusion of procaine amide (in addition to its increased concentration in the blood) results in profound electrolyte changes; acidosis is manifested by decreased pH and pCO_2; in addition there is a decrease in potassium, calcium and magnesium.

Beneficial effects of molar sodium lactate in procaine amide toxicity may result from a combination of the following: (a) decrease in plasma procaine amide levels, (b) improvement in acidosis, (c) decrease in serum potassium, and (d) the effect of lactate as a metabolic fuel. S. J. SHANE

Reversal of Cardiotoxic Effects of Quinidine by Molar Sodium Lactate.
S. BELLET *et al.*: *Am. J. M. Sc.,* 237: 165, 1959.

Because cardiotoxic effects of quinidine resemble those of hyperpotassæmia and molar sodium lactate reverses the cardiotoxicity of potassium, the effect of molar sodium lactate was studied in two series of dogs. In the control group, quinidine gluconate was given by continuous infusion until the animal died. In the second group, molar sodium lactate was administered at various stages of quinidine toxicity.

The cardiotoxic effect of quinidine as manifested by ECG changes and hypotension was repeatedly reversed by molar sodium lactate. However, in the far advanced stages of cardiotoxicity where a slow idioventricular rhythm was present and the blood pressure was close to zero, molar sodium lactate was either less effective or ineffective.

Beneficial effects of molar sodium lactate may be due to the following: (a) decrease in plasma quinidine concentration, (b) decrease in serum potassium with shift of pH to the alkalotic side, and (c) use of lactate directly for energy production. S. J. SHANE

Prolonged Administration of Chlorpromazine Hydrochloride.
F. J. AYD, JR.: *J. A. M. A.,* 169: 1296, 1959.

This report deals with 31 women and 19 men, aged 12 to 70, who had taken chlorpromazine for from two to four years. The daily dosage range as well as the total dosage showed wide variation from patient to patient. Minimum total dosage was 54,000 mg. and the maximum was 1,078,000 mg. Laboratory investigations on these patients included complete urinalysis, hæmatological studies and liver function tests. In some patients, the white blood cell count dropped as low as 3000 and the neutrophil proportion to 30%, but both returned to normal as therapy with chlorpromazine continued. Of the liver function studies, only the cephalin flocculation test showed changes in some patients, but the results were not significant and it is not known whether they were due to chlorpromazine or not. All the patients gained from 20 to 54 lb. in weight. Menstrual changes were frequently observed, especially when 500 mg. or more daily was given. All these patients showed symptomatic improvement, a significant finding in patients who had not benefited from previous forms of treatment and who had a poor prognosis. The author concludes that chlorpromazine can be administered for prolonged periods without risk of harmful effects. W. GROBIN

Less Commonly Recognized Actions of Atropine on Cardiac Rhythm.
K. H. AVERILL AND L. E. LAMB: *Am. J. M. Sc.,* 237: 304, 1959.

Atropine sulfate is well known as a potent cardiac parasympatholytic blocking agent, but these authors show that, in addition, there are three distinct phases of atropine action on the heart. These include an initial vagotonic effect, a transient period of vagal imbalance at different levels of the conduction system, and a final prolonged period of parasympathetic blockage. The changes seen during the *early* action of atropine are similar to those seen when vagal imbalance is produced by various simple respiratory procedures. Use might be made of this early action of atropine in the investigation of certain arrhythmias and conduction defects. It appears that, although the cardiac actions of atropine in the usual clinical doses are benign, serious arrhythmias and conduction defects may occur when it is combined with drugs such as neostigmine. S. J. SHANE

OBSTETRICS AND GYNÆCOLOGY

Rubella and Pregnancy.
H. OXORN: *Am. J. Obst. & Gynec.,* 77: 628, 1959.

In this series 47 women had rubella while they were pregnant. Nine of these were affected in the second and third trimesters and gave birth to normal children. Seven women who had rubella in the first trimester had spontaneous or induced abortion.

Thirty-one women who had rubella in the first trimester of pregnancy carried to term. Twenty-five of the children were normal and six babies were born with congenital defects. Of these six, one was born dead, two died at 3 weeks of age and three survived.

The incidence of abnormal babies who were carried to term after a maternal attack of rubella in the first trimester of pregnancy was 19% or one in five.

ROSS MITCHELL

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PROVINCIAL NEWS

BRITISH COLUMBIA

The recommendations of the Chant Royal Commission, appointed to examine educational matters in the province, contain a suggestion worthy of careful consideration.

It is recommended that pre-school children should be "scientifically screened" before admission to Grade one. This was based on recommendations from the British Columbia Branch of the Canadian Public Health Association, formed on doctors' and nurses' observations of physical difficulties, reading and speech problems and neurotic behaviour which can be traced to unfitness of a child to enter Grade one; the child has a sense of failure and this leads later to trouble.

Dr. J. F. McCreary, University of British Columbia dean of medicine, who is first and foremost a pædiatrician, has some pungent remarks to make about the facilities for study and treatment available, or rather lacking, in the Children's Health Centre.

He emphasizes the need for pædiatric psychiatry in the investigation of defects in children. He says, "There are probably five or six thousand children in British Columbia likely to constitute problems in the law courts, correctional institutions and mental hospitals of the next generation." The Child Guidance Clinic is inadequately staffed to meet this problem.

More specialized investigation by a cardiologist of heart defects in infants, to permit adequate examination and surgery, even within a few days of birth, is needed; "otherwise we are going to continue to lose more lives than we should, and do only half the job we should be doing." At present, he points out, waiting time for open heart surgery in Vancouver is between 14 and 15 months.

He calls for immediate expansion of the facilities of the Health Centre. We need, he says, a new sick children's hospital with modern facilities for research and diagnosis.

Dr. H. Rocke Robertson, who is leaving his position as head of the department of surgery at the University of British Columbia to take a similar post at McGill, was honoured by the McGill Society of Vancouver at a farewell garden party and barbecue on May 7. This was held at the home of Dr. D. L. Skinner and was largely attended.

Mr. Oliver Field, director of the Bureau of Investigation of the American Medical Association, is an old friend of ours in British Columbia. He has spoken before association meetings on quackery. He has an amazing collection of various gimmicks used by quacks, and has a great knowledge of the whole subject. He spoke on May 12 to a public meeting in the Vancouver Art Gallery under the sponsorship of the Canadian Arthritis and Rheumatism Society and the *Vancouver Province*.

The meeting was interrupted several times by hecklers, who were ardent supporters of the many-times exposed Hoxsey treatment for cancer. The most vociferous objector was our old friend, Mrs. Lydia Arsens from Victoria, who never misses an opportunity to hold forth on the merits of this thoroughly discredited "cure for cancer".

The new wing of the Burnaby General Hospital, built at a cost of $2,000,000, was opened by the Hon. Eric Martin, Minister of Health, on May 9. This will make a total bed capacity of 250 for the hospital. It will also provide 64 bassinets. There will be enlarged operating and laboratory facilities, and a new emergency department.

Speaking at the official opening, Mr. Martin called the 250-bed institution, which it is proposed later to expand to 600 beds, one of the most efficient in British Columbia.

This area in Burnaby is growing very fast in population, and hospital needs are growing also. We are not surprised to hear that the Board of Directors are already planning for a third unit, and it is intended that the hospital should eventually have a fourth unit.

Dr. Harold E. Taylor, head of the University of British Columbia department of pathology, was elected to the Executive Council of the International Academy of Pathology at the Academy's meeting at Boston, Mass.

May 11-16 was Arthritis Week in Victoria and great emphasis was being laid on the work of the Canadian Arthritis and Rheumatism Society, and the necessity for continual work and auxiliary methods of treatment.

In Victoria needy patients suffering from all forms of arthritis and rheumatism, who would otherwise be unable to obtain treatment, are treated free of charge by doctors provided through the Victoria Medical Society. The local clinic is financed through C.A.R.S. working in co-operation with Community Chest organizations.

Dr. Russell Henry Marshall and Dr. Peter H. Spohn have been elected to fellowship in the American Academy of Pediatrics.

At the annual meeting of the British Columbia Tuberculosis Association, Dr. G. F. Kincade, head of the Pearson Hospital and director of the tuberculosis division of the Health Department, gave some interesting details about the use of radiation in diagnosis.

Chest radiographs of the population at large are taken only when a tuberculin test has proved positive—and this test is done first. About one-third of the population shows a positive test. In patients over 40 routine x-ray examinations will probably be continued to catch early cases of lung cancer, etc.

The routine x-ray examination of patients on admission was cut 34% during 1958, partly because some persons refused this, partly because of the new policy adopted by hospitals and mobile x-ray units. Children and pregnant women will not be x-rayed unless a tuberculin test is positive, or for certain other definitive reasons. Routine radiography for tuberculosis will be confined to once a year. Groups are more closely selected; known contacts, homeless drifters and older persons are concentrated on. Improvements in x-ray technique which lessen exposure time, use of faster films, and better protection of machines against leakage have reduced the radiation received to "virtually" insignificant proportions.

Dr. Kincade noted that while positive tuberculin tests used to be extremely common, now only one-third of the population give positive tests.

Mr. L. A. Atkinson, chairman, gave some figures showing the steady decline of TB in British Columbia:

Only 71 persons died of tuberculosis in British Columbia last year, while 10 years ago 442 died. Hospital treatment has been greatly improved—but there are still 1000 people occupying hospital beds. The decline in tuberculosis amongst Indians has been spectacular. In 1948, 156 Indians died of tuberculosis, with only 16 deaths in 1958.

Both speakers warned against complacency. Tuberculosis is still a very serious disease in British Columbia—and Ontario, Saskatchewan and Alberta all have better figures than our own. In 1958 about 50 cases of active tuberculosis were admitted to hospital each month.

Dr. A. C. Waldie, Vancouver, has received a $500 bursary for postgraduate work, the Upjohn Scholarship for 1959, awarded by the College of General Practice of Canada at its recent meeting in Toronto. Dr. J. H. Kope of Enderby received a similar award.

Dr. S. Z. Bennett of Salmon Arm was the British Columbia recipient of another award of $500, sponsored by the Schering Company. Dr. Bennett will utilize his award to take a course of postgraduate training this summer at the University Hospital in Saskatoon.

The Hon. Eric Martin, Minister of Health for British Columbia, recently announced organization of a preventive program for special treatment of children suffering from rheumatic fever, with a view to forestalling or minimizing heart disease.

A committee representing the Canadian Medical Association (B.C. Division), the University of British Columbia department of pædiatrics, the B.C. Heart Foundation and the Provincial Health Department has drawn up plans for this program. While regional committees working with local health units will exercise immediate supervision, responsibility for the patient will remain with the physician, who will initiate and carry out treatment in co-operation with the local health services.

Penicillin will be made available by the Department of National Health and Welfare.

Public health nurses will be actively engaged in carrying out the program.

The plan is now in effect in five areas—Courtenay, Kelowna, Cloverdale, New Westminster and Burnaby—and will be extended if and when results justify this extension. J. H. MACDERMOT

ALBERTA

Dr. F. D. Locke of Lacombe, Alberta, has received word that one of his pictures has been accepted to be shown at the C.M.A.-B.M.A. art exhibit in Edinburgh. Dr. Locke has received awards at the divisional and national levels.

The *Edmonton Journal* recently ran an article on Dr. Van Stolk, who, after two years at Lambarene with Dr. Albert Schweitzer, has become resident in psychiatry at the University of Alberta hospital. Dr. Van Stolk studied at the University of Leiden, Holland, and graduated in medicine at the University of Cape Town, South Africa, after which he joined Dr. Schweitzer. While on leave to study at Harvard Medical School Dr. Van Stolk married. Dr. Schweitzer agreed with him that Equatorial Africa was not the place to raise a family.

Recently elected to membership in the American College of Physicians were five Albertans: Drs. J. A. L. Gilbert, C. B. Rich, Stanley Greenhill and Ludwick Sherman, all of Edmonton, and Dr. H. F. McInnis, Camrose.

According to an announcement by Alberta's Minister of Health, Dr. J. Donovan Ross, no more hospitals with a capacity of less than 25 beds will be built in Alberta. The reason given was that below this level adequate service cannot be given economically, and that at this level very few areas in the province will not have reasonably close hospital accommodation.

Dr. J. S. Thompson, who has served as executive secretary of the faculty of medicine at the University of Alberta since 1953, has been appointed assistant dean of medicine. The appointment becomes effective September 1, 1959.

The first Dr. W. H. McGuffin memorial lecture was delivered at a luncheon meeting of the Calgary and District Medical Society which was held in conjunction with the April refresher course. The speaker was Dr. Ivan L. Smith, director of the Ontario Cancer Foundation, London, Ontario. Dr. McGuffin, after graduating in medicine from the University of Western Ontario in 1910, practised medicine in Calgary from 1911 to 1949, the years subsequent to 1918 being spent in the specialty of radiology. Dr. McGuffin was widely honoured as a radiologist and served as president of the Canadian Radiological Society, the Radiological Society of North America and the Canadian Association of Radiologists. With Dr. John McEachern he organized the Alberta Cancer Society, which later became the Alberta branch of the Canadian Cancer Society. Dr. McGuffin's widow attended the memorial lecture.

Members of the Calgary and District Medical Society who take office this month are: past president, Dr. M. D. Mitchell; president, Dr. L. I. Mitchell; vice-president, Dr. H. C. Worrall; and secretary, Dr. D. R. Buchanan. New executive members are: Dr. H. McEwen and Dr. A. B. Ostrander. W. B. PARSONS

SASKATCHEWAN

At the University of Saskatchewan Convocation, three honorary degrees were conferred. E. C. Leslie of Regina, Past President of the Canadian Bar Association and an alumnus of the University, received a D.C.L. Dr. H. E. Johns of Toronto and Dr. Pierre Dansereau of Montreal received an LL.D. degree.

It is of interest to note that an $11,000 grant over a three-year period has been awarded by the Milbank Memorial Fund of New York to the University of Saskatchewan College of Medicine. These funds will be used to give selected third-year medical students at the University of Saskatchewan an opportunity to study community health problems.

The public health preceptorship scheme will be initiated along with the College of Medicine's existing preceptorship scheme in rural general practice, under which a third-year student spends two weeks with a general practitioner in a rural centre. With the new scheme, up to four students will

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be chosen annually, and the selected ones will receive an award of $750 and travel and other expenses. They will serve their general practice preceptorship the first two weeks in June, and from mid-June to the end of August will serve in one of Saskatchewan's health regions, working in the various departments and assisting in various activities. The students will have an opportunity for some clinical experience in the hospital and for continuing observation of their preceptor's general practice.

The Milbank grant also provides funds for travel for the members of the University's Department of Social and Preventive Medicine, and further studies in community health problems may be carried out.

The Saskatchewan Dental College plans to seek changes in the new Dental Profession Act at the next session of the Saskatchewan Legislature. This decision was reached at the Annual Meeting of the Saskatchewan College of Dental Surgeons held in Saskatoon during April. It was reported that Saskatchewan is "now the only place in the world where bootleg dentistry has been placed in such a favoured position".

It was also stated that the Saskatchewan Legislature had changed the Act governing the dental profession, including the definition section regarding dentistry. It is felt by the Dental College of this province that "this was a seeming attempt to confine the practice of dentistry to simply the filling and extraction of teeth". It was considered, so the report stated, that the whole field of prosthetic dentistry was being thrown open to anyone: "anyone, your barber, your plumber, your garage mechanic, your newspaper editor, or even your M.L.A. may engage in any activity embraced in the field of prosthetic dentistry. Fortunately the Legislature did not exclude a dentist from engaging in this field."

It is understood that under the new Act, the only basis on which persons could be prosecuted for the illegal practice of dentistry would be if they did denture work without having a certificate of oral health for the person receiving dentures. Under the Act, a certificate of oral health must be obtained from a registered member of the Saskatchewan Dental College, or the College of Physicians and Surgeons of Saskatchewan.

The meeting was told that it is felt that there was a strong "anti-profession" bias existing among the members of the Legislature. G. W. PEACOCK

ONTARIO

The Ontario Medical Association has elected Dr. William W. Baldwin, Brooklin, president; Dr. William W. Wigle, Dryden, president-elect; Dr. Ian W. Davidson, Sudbury, chairman of council; and Dr. R. H. McCreary, Arnprior, honorary treasurer.

At the annual banquet, senior memberships in the Canadian Medical Association were presented to Dr. Freeman A. Brokenshire, Windsor; Dr. George A. Campbell, Ottawa; Dr. W. E. Gallie, Toronto; Dr. T. Clarence Routley, Toronto; and Dr. H. M. Yelland, Peterborough. Dr. Campbell was also awarded an O.M.A. life membership.

O.M.A. honorary memberships were presented to Dr. C. H. Best, Dr. Herbert A. Bruce and Dr. Boyd Neel, all of Toronto.

O.M.A. life memberships were presented to Dr. George B. Burwell, Renfrew; Dr. James E. Carson, Brantford; Dr. Frank R. Clegg, London; Dr. Francis L. Eberhart, Meaford; Dr. John L. King, Galt; and Dr. Russell B. Robson, Windsor.

The 13-storey addition to the Toronto General Hospital has been officially opened by Premier Frost. This addition gives the hospital a gain of 325 beds, bringing the total to 1750 beds. To complete the addition $16,000,000 was raised, of which $12,400,000 was spent on the building, $1,375,000 on equipment and about $250,000 on the partial rehabilitation of the original building and the Wellesley division. Gifts from 49,600 subscribers totalled more than $8,500,000. The federal government made a grant of $1,000,000.

Dr. E. F. Brooks, physician in chief, St. Michael's Hospital, Toronto, has been elected a Fellow of the Royal College of Physicians, London.

Dr. W. C. McMurray, assistant professor of biochemistry in the University of Saskatchewan, has been appointed to Canada's first research professorship in biochemistry for basic research relating to mental deficiency, at the University of Western Ontario.

The funds to establish this post, $12,000 a year for five years, were granted to the Ontario Association for Retarded Children by the Junior Red Cross of Ontario. LILLIAN A. CHASE

Sir Stewart Duke-Elder, Ph.D., F.R.C.S., has been awarded the Charles Mickle Fellowship for 1959 by the University of Toronto for his outstanding research in ophthalmology. Sir Stewart was created a Knight in 1933 and later was made a Knight Commander of the Royal Victorian Order and a Knight Grand Cross of the Royal Victorian Order. He has been Surgeon-oculist to the Queen since 1952 and prior to this was Surgeon-oculist to King George VI.

Sir Stewart, Director of Research at the University of London's Institute of Ophthalmology, came to Toronto on May 21 to lecture on "Recent advances in diagnosis and treatment of glaucoma" at the Charles H. Best Institute.

The Mickle Fellowship is the income from $29,000 bequeathed by the late Dr. W. J. Mickle, and is awarded annually to the member of the medical profession who is considered by the Council of the University's Faculty of Medicine to have done most during the preceding ten years to advance sound knowledge of a practical kind in medical art or science.

Sir Stewart pioneered the early research into the cause of glaucoma, which is the commonest cause for blindness in the Western world.

Kingston Notes

Dr. R. W. Ian Urquhart, chairman of the Ontario Hospital Services Commission, Toronto, received the honorary degree of Doctor of Laws from Queen's University at the Annual Medical Convocation on Saturday, May 30. In presenting Dr. Urquhart to Vice-Chancellor Mackintosh, Dr. G. H. Ettinger, dean of the Faculty of Medicine, said:

"Mr. Vice-Chancellor, The Senate has directed me to present to you that he may receive at your hands the degree of Doctor of Laws, *honoris causa,* Richard William Ian Urquhart, university teacher, investigator,

soldier, industrial physician, who brings to his post as Chairman of the Ontario Hospital Services Commission the confidence of the profession of medicine that as magician for the people, the government, and the profession, he will balance hospital budgets while keeping empty beds always in view, pull free diagnostic procedures out of hats, change indigence into fees-for-service, and convert for the Ontario citizen the threat of disastrous costs to the monotonous payment of instalments."

In his convocation address Dr. Urquhart urged the graduates to "seek out the far horizons", and paid tribute to Dean Ettinger for his contributions as a research scientist in physiology.

"In the old days the home was the battlefield," said the speaker. "Today so complicated are the procedures involved, so dependent are they on the knowledge and skills of a number of people, that the battlefield has been transferred to the hospital. Only there can medical forces be mobilized effectively to prevail against suffering and disease.

"It is for this reason that I am happy to be involved in the administration of the new program of hospital insurance in this province. It makes available to everyone, rich and poor alike, on an insured basis, hospitalization without limit to those who require the resources of a hospital for the treatment of their disease. True, we need more hospital beds and facilities of every kind. These, however, are the shared responsibility of community and governmental agencies; working shoulder to shoulder they can be produced, but it will take time.

"May God give you the ability to seek out the far horizons."

R. C. BURR

QUEBEC

The 15th Biennial Meeting of the Canadian Hospital Association was held at the Queen Elizabeth Hotel in Montreal on May 12. With nine out of ten provinces now committed to hospital insurance schemes, it is understandable that most of the presentations dealt with economic and administrative as well as professional problems such as length of stay in hospital, availability of beds and chronic versus acute illness. Hospital use has gone up consistently throughout the country with increasing use of insurance schemes, and now, in part because the doctor need no longer worry whether the insured patient can afford to go to a hospital, this has still further increased hospital use. An interesting report dealt with a Michigan Blue Cross study by doctors of 12,000 consecutive admissions. This showed that 15% of hospital days were unnecessary to the safety or recovery of the patient. Insured patients misused hospital stay twice as often as those who paid their hospital bill. Dr. E. H. Lossing of Ottawa, principal medical officer in charge of health insurance, reported on the hospital insurance plan now in effect in seven Canadian provinces, projected in two more, and from which Quebec still remains aloof. He emphasized how few difficulties of any real importance have so far been encountered in view of the magnitude and complexity of the scheme. Other important problems were referred to, presented or discussed in detail, including civil defence health services, the training of nurses and accreditation of nursing schools. Stanley W. Martin of Toronto was elected president; Chief Judge Nelles V. Buchanan, Edmonton, first vice-president; Harvey E. Taylor, Port Alberni, B.C., second vice-president; and Dr. John E. Sharpe, Toronto, treasurer.

The Board of Directors of the National Cancer Institute of Canada met in Montreal on May 19. Two Montrealers were elected to membership: Mr. G. Arnold Hart, president of the Bank of Montreal, and Dr. Rocke Robertson, chairman of the department of surgery, McGill University, and surgeon-in-chief, Montreal General Hospital. Announcement was made of an agreement to establish the first full-time cancer research centre in Montreal. The contract which was signed by the Montreal Cancer Institute, the University of Montreal and the National Cancer Institute provides for a regular flow of funds to operate the research laboratories of the Montreal Cancer Institute. It also gives senior members of the Institute faculty status at the University of Montreal. Principally, under this contract, the University of Montreal agrees to provide the research scientists, the Montreal Cancer Institute provides the laboratory facilities and the National Cancer Institute guarantees to make sufficient funds available to finance the operation. The financial liability, however, is limited to research and does not include costs of operating the detection, diagnostic or treatment centres of the Montreal Cancer Institute.

The Montreal Cancer Institute was founded 10 years ago at the Notre-Dame Hospital and is directed by Dr. Louis-Charles Simard, who is associate professor of pathology at the University of Montreal. During its period of existence and largely because of the untiring efforts of its director, the Montreal Cancer Institute has acquired a world-wide reputation for its biochemical research in pathological and analytical chemistry and in biophysics and histochemistry, all related to the general problems of cancer. It is very pleasing that this effort is being recognized in terms of long-term financial support.

It was recently announced by the Cancer Research Society of Montreal that they have collected $40,320 for cancer research and are awarding this to research centres in the city. At the annual meeting of the Society at which the various awards were announced, Dr. Lloyd Stevenson, dean of the Faculty of Medicine at McGill University, addressed the gathering on the duty of society to aid research. He praised the work that had been done by voluntary societies in raising money for research and emphasized that the whole of society, and not only scientists, is responsible for medical research.

The annual meeting of la Société Médicale de Montréal was held in the Social Centre of the University of Montreal on May 2, and took the form of an all-day scientific program, plus a luncheon at noon and a reception and dinner in the evening. There were ten major presentations, and speakers included three experts from out of town. Dr. M. Magin Sagarra, assistant professor of obstetrics and gynecology, New York Medical College, presented experiences on problems of infections in the pelvis; Dr. M. Jean Grandbois, professor of dermatology at Laval University, spoke on infections of the scalp; and Dr. M. Dominique Conway, professor of pædiatrics at the University of Ottawa, discussed staphylococcal pneumonia in infants. The executive of the Society for the coming year in-

cludes Dr. Jean-Paul Legault, president; Dr. Albert Roger, vice-president; Dr. Gérard Morin, second vice-president, and Dr. Georges Leclerc, secretary-general. During the session it was announced that the membership of the Society now stands at 1131 members, the highest figure achieved since the Society was founded in October 1940.

A unique feature at the annual inspection of No. 1 Battalion, R.C.A.M.C. (Militia), at the Lacombe Armory in Montreal, held on May 12, was the presentation to Mrs. F. A. C. Scrimger of a portrait depicting the battle where her husband's valour won him the highest military decoration in the Commonwealth, the Victoria Cross. The late Dr. Scrimger was medical officer to the 14th Battalion, C.E.F., when he was awarded the Victoria Cross for his bravery in Belgium on April 25, 1915. At that time he held the rank of Captain, and was later promoted to Lieut.-Colonel. He died on February 13, 1937. The portrait will be forwarded by Mrs. Scrimger to the Victoria Cross Room at the Royal Medical Corps College, Millbank, England. There, a place of honour is reserved for the plaques or portraits commemorating all the medical officers in the Commonwealth Forces who were awarded the Victoria Cross. Presentation of the portrait was made by Brigadier C. Thompson, honorary colonel of No. 1 Battalion R.C.A.M.C. (Militia).

At the recent annual meeting of the Montreal Neurological Institute, Dr. Wilder Penfield reported on difficulties of securing adequate funds to continue an active research program concurrent with treatment at the Institute. He emphasized that what is needed is a permanent research endowment. Since then the Canadian Legion has volunteered its services to help build a permanent research fund for the Institute. Details of this arrangement will be worked out later. Legion officials state that the group feels highly honoured to undertake this work on behalf of the Institute. The funds will be coming from the Legion's annual "March of Dimes", held every year in January. It is interesting to note that the drive last year by Quebec veterans netted $118,000. In the past, most of these funds have been directed towards the care and rehabilitation of polio sufferers and research into hæmophilia.

This year the annual Convocation Days at the University of Montreal as well as at McGill University were held on the same day, May 29. At McGill, 98 graduated in the Faculty of Medicine, compared with 119 a year ago. It is interesting to note that the graduate with the highest standing was Thomas Craig, a former U.S. Navy officer of Lynbrook, N.Y. He received the Holmes Gold Medal for highest standing in all subjects and the Alexander D. Stewart Memorial Prize for highest qualifications in the practice of medicine, and was the co-holder of the Francis Williams Scholarship in clinical and medical studies. He is also a 27-year-old father of three children. Another unique feature was the graduation of Dick Baltzan of Saskatoon. He is the last of three brothers who have graduated from the Faculty of Medicine at McGill. Their father, Dr. David M. Baltzan, is a McGill graduate of the class of 1920.

The Industrial Medical Association of the Province of Quebec held their annual meeting in Montreal on May 29. Dr. Milton G. Townsend was elected president, Dr. Eustace Morin, first vice-president, and Dr. L. C. Haslam, second vice-president. Dr. Lloyd Birmingham of Montreal was elected secretary for the coming year.

Dr. Kenneth J. MacKinnon has been appointed urologist-in-chief at the Royal Victoria Hospital in Montreal, effective July 1. He is a graduate of Dalhousie University and joined the hospital in 1953. In 1956 he was appointed director of urology at the Montreal Children's Hospital. A. H. NEUFELD

NOVA SCOTIA

Dr. A. D. R. Lapp has retired from the D.V.A. Hospital at Camp Hill. Dr. Lapp spent from 1946 to 1949 in association with the Department of Veterans Affairs, first in Cornwallis and later at Camp Hill Hospital.

FORTHCOMING MEETINGS

CANADA

WORLD MEDICAL ASSOCIATION, 13th General Assembly, Montreal, Que. (Dr. Louis M. Bauer, World Medical Association, 13 Columbus Circle, New York 19, N.Y.) September 7-12, 1959.

SOCIETY OF OBSTETRICIANS AND GYNÆCOLOGISTS OF CANADA, Annual Meeting, Mont Tremblant Lodge, Mont-Tremblant, Que. (Dr. F. P. McInnis, Secretary, 280 Bloor St. West, Toronto 5, Ont.) September 10-13, 1959.

CANADIAN OPHTHALMOLOGICAL SOCIETY (SOCIÉTÉ CANADIENNE D'OPHTALMOLOGIE), Annual Meeting, Sheraton-Brock Hotel, Niagara Falls, Ont. (Dr. R. G. C. Kelly, Secretary, 90 St. Clair Avenue West, Toronto 7, Ont.) October 6-8, 1959.

CANADIAN OTOLARYNGOLOGICAL SOCIETY (SOCIÉTÉ CANADIENNE D'OTOLARYNGOLOGIE), Annual Meeting, Sheraton-Brock Hotel, Niagara Falls, Ont. (Dr. Donald M. MacRae, Secretary, 324 Spring Garden Road, Halifax, N.S.) October 9 and 10, 1959.

THE CANADIAN SOCIETY FOR THE STUDY OF FERTILITY, Annual Meeting, Queen Elizabeth Hotel, Montreal, Quebec. (Dr. Jean F. Campbell, Secretary-Treasurer, 238 Queen's Ave., London, Ont.) October 23 and 24, 1959.

UNITED STATES

2ND WORLD CONFERENCE ON MEDICAL EDUCATION, Chicago, Ill. (Dr. Louis M. Bauer, World Medical Association, 10 Columbus Circle, New York 19, N.Y.) August 30-September 4, 1959.

INTERNATIONAL COLLEGE OF SURGEONS, 24TH ANNUAL CONGRESS OF NORTH AMERICAN FEDERATION (United States, Canadian and Mexican Sections), Palmer House, Chicago. (Dr. Ross T. McIntire, Executive Secretary, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Ill.) September 13-17, 1959.

OTHER COUNTRIES

PAN AMERICAN MEDICAL ASSOCIATION, 10th Congress, Mexico City, Mexico. (Dr. Joseph Eller, Executive Director, Pan-American Medical Congress Association, 745 Fifth Ave., New York 22, N.Y.) October 19-31, 1959.

VI PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY, Caracas, Venezuela. (Dr. R. G. C. Kelly, 90 St. Clair Ave. West, Toronto 7, Ont., Assistant Secretary.) January 31-February 7, 1960.

BOOK REVIEWS

HEALTH IN INDUSTRY. Donald Hunter. 288 pp. Illust. Penguin Books Ltd., Harmondsworth, Middlesex, 1959. $0.80.

For several decades the students at the London Hospital have had a unique privilege—that of being taught by a man whose interests range far beyond the narrow confines of the hospital, and who has successfully combined the attributes of a skilful clinician with a first-hand knowledge of industrial medicine. This dynamic teacher, Donald Hunter, has now produced what must be the best students' textbook of industrial medicine in the world. Canadians who have encountered Donald Hunter will scarcely need to be told that the book is a delight to read and packed with information from start to finish. Nor will they need to be told that the author has the answer to the critics who complain of the de-humanization of medicine, for the whole book is a reflection of his interest in people as persons, and in everything that affects their everyday lives.

Hunter starts with a broad historical survey of industrial medicine, passes on to legislation (this of course means legislation in Britain, and some modification is needed to translate the chapter into Canadian terms), accidents at work, and the various occupational diseases. As he has been doing for many years, Hunter emphasizes prevention rather than treatment. He also emphasizes the happiness of the individual, and much of the book can be read with profit by sociologists, politicians, management and labour. At eighty cents, this must be the medical book buy of the year.

TRIFLUOPERAZINE — CLINICAL AND PHARMACOLOGIC ASPECTS. 44 Contributors. 214 pp. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1958. $3.50.

In this book some 25 papers on trifluoperazine are collected and grouped under broad headings according to the clinical syndromes in which this neuroleptic drug has been tried. Most of the writers are from state mental hospitals, some are from university psychiatric centres, and three papers are Canadian. From this book one can learn a great deal about the drug's usefulness and its difficulties. Thoughtful comparison of the papers teaches something else too.

In any appraisal of the neuroleptic drugs very careful consideration must be given to the question which the study is designed to answer, to the structure of the "research study" itself, to the many variables, and to the "controls". This has not always been done by the authors, and the result is sometimes seen in sweeping generalities and contradictions. Yet some of the studies described were well planned. One of the best is from Topeka State Hospital where Paul E. Feldman, Director of Research, has attempted to compare trifluoperazine with chlorpromazine. He concludes that "in many of its effects it is similar to chlorpromazine", yet there are marked contrasts too.

A final statement of where this drug should be used, and where another of the many neuroleptics is the drug of choice, is not yet possible. Yet the book will give the practitioner a clear picture of the many ways in which trifluoperazine can be used, a clear picture of side effects, of their control and of the dosage schedules possible. It is not a book that conclusively defines the indications and mode of action of a new drug. It is a collection of papers by men who have been using trifluoperazine, and the reader will gain from their experience.

LESIONS OF THE LOWER BOWEL. Raymond J. Jackman, Head of the Section of Proctology, Mayo Clinic, Rochester. 347 pp. Illust. Charles C. Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. $17.00.

This first edition, published simultaneously by Blackwell of Oxford, Charles C. Thomas of Springfield and the Ryerson Press, Toronto, is concerned principally with the diagnosis of intrinsic, intramural and extrinsic lesions of the lower part of the large intestine.

When one considers that 70% of the pathology of the lower bowel is within the reach of a 25-cm. sigmoidoscope, this timely volume is an essential in the library of any doctor dealing with health assessment.

The technique of sigmoidoscopic examination is carefully explained anatomically, the pitfalls are outlined, and the procedure in current use at the Mayo Clinic is described. The chapter on physiology of the lower bowel is unique and its perusal rewarding. The author has drawn, from his wide experience of pioneer work in colour photography through the sigmoidoscope, an abundance of colour plates illustrating the fact that a picture is worth a thousand words. An extensive table of contents and a cross-index cover almost every condition found in the lower bowel. A careful history followed by an examination with a well-trained finger, and by use of hand and eye in guiding a sigmoidoscope, before blindly ordering an x-ray examination of the lower bowel is stressed. The lesions which the author has found, seen and recorded in colour for all to see are a feature of this long-overdue book. The author leaves the impression with the reader that a sigmoidoscopic examination is just as important a part of a physical examination as a chest x-ray examination and even more so, especially because of the importance of early diagnosis of an adenoma, which is a precursor of carcinoma. The technique of fulguration of these early lesions is outlined in detail. Practical suggestions here and there are interspersed with the main theme stressing diagnosis. This volume is the culmination of many years of exhaustive work, and the author is to be commended for his very useful storehouse of information and reference regarding diagnosis of lesions of the lower bowel.

TREATMENT IN INTERNAL MEDICINE. Harold Thomas Hyman, Riverview Hospital, Red Bank, N.J. 609 pp. Illust. J. B. Lippincott Company, Philadelphia and Montreal, 1958. $12.50.

This book can be recommended as an unusually well organized, lucid account of therapeutics for general physicians. The dogmatic style saves words and leaves no doubt about the opinions of the author. The approach is practical, vigorous and resourceful. Scattered throughout the informative text one finds many wise observations about doctors, patients and other aspects of medical practice. Undergraduate students will find here a valuable guide through the maze of modern therapy. General physicians will thank Dr. Hyman for his advice on all the common and most of the uncommon problems of treatment. The author is to be congratulated on the successful outcome of a laborious task.

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STRABISMES, HETEROPHORIES et PARALYSIES OCULOMOTRICES (Strabismus, Heterophorias and Oculomotor Paralysis). René Hugonnier. 748 pp. Illust. Masson & Cie, Paris, 1959. Paper 7.500 fr., cloth 8.500 fr.

Ce volume est un traité élaboré sur le sujet. Il est divisé en six parties. La première traite de l'anatomie et de la physiologie; la deuxième étudie en détail les strabismes et hétérophories. Une troisième partie s'attache à l'étude des déséquilibres oculo-moteurs d'origine paralytique. Dans la section anatomie et physiologie—et ceci cadre bien avec le sujet traité—l'auteur donne surtout de l'importance à l'étude des muscles oculo-moteurs ainsi que des voies et nerfs oculo-moteurs. L'action particulière de chacun des muscles droits et obliques de l'œil est décrite en détail de même que le mécanisme, le développement et le rôle de la vision binoculaire. Sur le reste, il ne donne que des notions. Dans une quatrième partie, l'auteur étudie les différentes méthodes d'examen; examen objectif d'un déséquilibre oculo-moteur, d'un strabisme, d'une hétérophorie, etc. Ainsi qu'il le dit, il insiste "surtout avec détails" sur les méthodes qu'il emploie personnellement dans la pratique de tous les jours. Les dernières parties de l'ouvrage sont consacrées aux différentes méthodes de traitement. La section du traitement non chirurgical comporte plusieurs chapitres consacrés au traitement orthoptique. Celle du traitement chirurgical décrit les différentes techniques opératoires et parle des indications et contre-indications opératoires des différents déséquilibres oculo-moteurs.

En résumé, il s'agit d'un volume complet sur *l'étude théorique* des déséquilibres moteurs de l'œil. On ne pourrait pas dire de cet ouvrage qu'il serait très utile au praticien puisqu'il traite exclusivement d'un problème particulier — sous ses différents angles — à l'ophtalmologiste. La lecture en sera par contre très profitable au jeune médecin qui se destine à l'ophtalmologie; elle ne remplacera pas pour celui-ci la pratique médico-chirurgicale de sa future spécialité mais elle la complètera avec avantage. Enfin, pour l'ophtalmologiste, cet ouvrage constituera un excellent rappel des notions qu'il savait déjà et peut-être de celles qu'il avait oubliées.

PREVENTIVE MEDICINE IN WORLD WAR II. Vol. IV, Communicable Diseases Transmitted Chiefly through Respiratory and Alimentary Tracts. Published under the direction of Major General S. B. Hays, The Surgeon General, United States Army. 544 pp. Illust. Office of the Surgeon General, Department of the Army, Washington, D.C., 1958.

This volume, together with two further volumes of the Preventive Medicine series still to follow, records the story of communicable diseases in World War II in the United States Army. It is obvious in reading this fascinating history that the primary aim of the authors is to demonstrate how much of a factor communicable diseases were in the conduct of military operations at that time. A secondary aim is to define those particular features which characterized the communicable diseases in military practice as contrasted with usual civilian conditions. The experiences of World War II from which they were able to draw were comprehensive, without parallel in the history of warfare. World War I was the first United States experience, in which deaths from disease were fewer than deaths from battle casualties. This, however, was true only for troops in the active European campaign of 1918. For all men under arms, the rate was still slightly greater for disease than for battle casualties. In contrast, World War II brought about a complete departure from previous experience with a health record never approached previously in any war. The ratio of deaths from disease to those from battle injuries was 0.07:1.

The story in this volume is presented in three parts. The introduction presents general considerations of modes of transmission. Part II deals with diseases transmitted chiefly through the respiratory tract. Part III presents diseases transmitted chiefly through the alimentary tract. The authors selected to present the difficult chapters were obviously men of wide experience as well as distinction in their special fields. The actual experiences of World War II certainly justify the emphasis which military medical officers continue to place on the significance of communicable diseases. The experiences presented include repeated threats of the great pandemic diseases; the occurrence of epidemics, even under the best of conditions; and the strange problems brought by modern warfare, characterized by rapid movement and wide dispersal of resources. Well-known infectious diseases that had been carefully evaluated and adequately controlled under conditions of the American environment took on new significance when encountered in other parts of the world. A lasting impression in the story of this volume is the steady erosion of manpower brought about by everyday infections, losses which become evident when communicable disease is measured in terms of non-effectiveness and of the permanent injury which leads to lasting disability. The deaths that these diseases cause are not the sole concern nor do they always provide a reasonable basis for judgment in both military and civilian practice of medicine and public health.

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MEDICAL NEWS *in brief*

(Continued from page 115)

THE PHONOCARDIOGRAM IN EVALUATION OF MITRAL STENOSIS

For some years there has been debate as to the value of the interval between onset of QRS complex and the earliest vibration of the first heart sound (Q-1 interval) in the assessment of mitral stenosis. Similar controversy has existed with regard to the significance of the interval between the onset of the second sound and the beginning of the opening snap.

In a study by Donnelly, Maha and Orgain (*J. Thoracic Surg.*, 37: 200, 1959), the value of phonocardiography in selecting candidates for mitral commissurotomy was assessed in a series of 47 patients submitted to operation. The "corrected" figures for the Q-1 intervals , 2-OS intervals, and Q-1 minus 2-OS values were compared with the size of mitral orifice found at operation. Appreciable correlation was evident between valve size and both the 2-OS interval and the Q-1 minus 2-OS value. No significant correlation was observed between the Q-1 interval and valve size. Postoperative observations in 17 patients revealed shortening of the Q-1 time in five patients, lengthening of the 2-OS interval in 14 patients, and decrease in Q-1 minus 2-OS value in 13 patients, the changes being greater in those patients with more severe mitral stenosis. When both the 2-OS interval is less than 0.09 second and the Q-1 minus 2-OS value is greater than -1.0, the likelihood of significant mitral stenosis is great. Fewer predictive errors in valve size are made when the values observed in a single patient satisfy both indices rather than either index used alone as a criterion.

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TRENDS IN CANCER DEATH RATES AND CURE RATES

E. C. Hammond (*Ann. Int. Med.*, 50: 300, 1959) points out that, among females, the age-standardized cancer death rate has been on the decline in the United States and several other countries for the last decade or longer. On the other hand, the rate for males is still increasing. Most of this increase among males is due to the phenomenal rise in the death rate from lung cancer.

He emphasizes that the death rate from cancer of the uterus is declining quite rapidly in the U.S.A., presumably as a result of control activities. The death rate from stomach cancer is declining, apparently as a result of a decline in incidence rates. The reason for this is unknown. There is also evidence that the five-year survival rate for cancer has markedly improved during the past decade or two. The greatest improvement has apparently occurred for cancer of the colon, rectum, cervix, uteri, corpus uteri and prostate, and, to a lesser degree, for cancer of the bladder.

It is estimated that about one-third of those who develop cancer in the United States today will survive for five years, a considerable improvement over the one-

quarter being saved a decade or two ago.

Unless some practical method of prevention is discovered and applied, the author considers that the annual number of new cases of cancer per year in the United States will almost certainly rise steadily during the next 50 years as a result of the growth and aging of the population. This means that the need for medical care as well as facilities for cancer patients will inevitably increase. On the other hand, there is reason to believe that the cure rate can be improved (perhaps up to as high as 50%) by more effective use of present knowledge for the detection, diagnosis and treatment of cancer.

TREACHEROUS TRANQUILLIZERS

Shaw and Felts (*Am. J. M. Sc.*, 237: 141, 1959) decry the promiscuous use of the modern psychopharmacological agents known as "tranquillizers". Criteria are put forward which should determine when the use of a chemotherapeutic tranquillizer is indicated and define the effects that it should produce in the individual case.

The authors declare themselves to be in accord with the recommendation of the American Psychiatric Association that tranquillizers should not be used if the patient has not had a medical investigation capable of establishing the factors in the particular case. In their conclusions, they state that "equanimity, tranquillity and serenity of the spirit are to be found in the depth of the individual personality and not in a bottle in a drug store. It is possible that our civilization is moving towards well-formulated objectives through a period of ideologic controversy. But what civilization in the history of humanity has differed in this respect from ours? That is, what civilization has not progressed by repeated trial and error from one crisis to the next? If crises produce tensions (and vice versa), then the energies of these tensions should be used constructively in the resolution of the crisis, in such a manner that human impulses shall become a positive force in the service of objectives of high value. Anxiety is like the smoke that precedes the fire. The fire can be used to great value in our daily life as a source of energy. But if it rages and escapes all rational boundaries, the consequence is a conflagration. Tranquillizers can be prescribed judicially to prevent or extinguish a fire at the margin of the forest but they should not be employed to combat a general invasion. It is not proper to use tranquillizers to remove completely all traces of anxiety, so long as it is this anxiety from which is derived the clear flame of ambition and of success. Tranquillity of spirit is transitory. It should not be sought as an objective *per se*. It should be used primarily as a medium to maintain our capacity to live and to continue to live, to hold our ground for the present and for the future, full of enthusiasm and without regret for past happenings."

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Canad. M. A. J.
July 15, 1959, vol. 81

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MEDICAL NEWS *in brief*

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TUBERCULOSIS IN ISRAEL

The morbidity and mortality trends from tuberculosis in Israel during the years 1947-1957 showed that with the increased immigration there was a rise which reached a peak about 1950-1951, and since then has shown a steady decline in both rates to almost the levels of 1947. The rise was due to an unselected immigration of 687,000 Jews who arrived in the country between 1948 and 1951. The immigrants belonged to various groups such as Eastern European, North African, Yemenites, Iraqis and other Asian groups. The author has prepared tables showing group specific morbidity and mortality rates of the various groups of immigrants. The Yemenite Jews and native Israeli Arabs were found to have a low infection rate but also a low resistance. North African, Near Asian and native Israeli Jews had a low infection rate and a high resistance. Eastern European Jews had a high infection rate and a high resistance to tuberculosis. The exception to this was the Eastern European Jews, whose resistance had been lowered during the war and their experience in Europe. Among the Arabs the Bedouins were found to have the lowest resistance and the highest morbidity rates.—S. Btesh: *Israel M. J.*, 17: 245, 1958.

EFFECT OF CARDIAC ARRHYTHMIAS ON CORONARY AND SYSTEMIC CIRCULATIONS

Comparative measurements of coronary artery and sinus flow, coronary blood pressure and systemic blood pressure, cardiac output and venous pressure were made by Corday *et al.* (*Ann. Int. Med.*, 50: 535, 1959) in animals during regular sinus rhythm, premature auricular and ventricular systoles, auricular tachycardia, flutter and fibrillation, and during ventricular tachycardia and fibrillation. Coronary artery flow was often reduced by these arrhythmias. Coronary sinus flow was also reduced but not to the same degree. Transient compensatory mechanisms attempted to maintain myocardial blood supply in rapid tachycardias if the systemic blood pressure and cardiac output were not too seriously compromised. Brachial artery tracings in human patients revealed a significant lowering of systemic blood pressure, similar to that in the experimental animal after premature atrial and ventricular systoles and during atrial fibrillation, flutter and tachycardia with rapid ventricular rates.

Coronary artery flow diminished in a linear fashion as the systemic pressure decreased. Therefore, if hypotension is present during attacks of rapid tachycardia of auricular or ventricular origin, it is advisable to restore the blood pressure with vasopressor drugs until other antiarrhythmic agents take effect. Vasopressor drugs themselves often promptly abolish atrial tachycardia, flutter and fibrillation, ventricular tachycardia and premature atrial systoles. It was found that the antiarrhythmic effect of pressor drugs was not mediated solely through the vagus nerve, but also by a direct effect on the heart. An explanation of the difference

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MEDICAL NEWS *in brief*

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between "benign" and "malignant" ventricular tachycardia is offered. In the more benign cases, the ectopic focus is nearer the cardiac apex. Most of the tachycardias studied were found to cause a decrease in coronary flow, or did not maintain coronary flow sufficiently to meet the increased nutritional demands resulting from the tachycardia. They should therefore be treated promptly, especially in patients with coronary artery disease.

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INTERNATIONAL JUBILEE CONFERENCE OF "THE ORANGE CROSS"

The Royal National Society for Life-saving and First Aid to the Injured, "The Orange Cross", will mark its 50th anniversary by holding an International Jubilee Conference at Scheveningen, the seaside resort of The Hague, September 10-12, 1959. The chief emphasis of the deliberations will be on resuscitation, burns, and electric shock. A series of seven case histories will present new or special developments relating to first aid in accidents. The program will also include international first aid competitions, a formal meeting to reactivate the "Association internationale de sauvetage et de premiers secours en cas d'accidents", and demonstrations of rescue work on land, at sea and in the air. The official languages will be English, French, German and Dutch. At the meetings simultaneous interpretation will be provided. Further information from: H. J. Oosterhuis, Secretary, International Jubilee Conference "50 Years Orange Cross", 14, Burgemeester de Monchyplein, The Hague, Netherlands.

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VACCINATION AGAINST POLIOMYELITIS WITH LIVE VIRUS VACCINE

The value of attenuated live poliovirus vaccine is still not established. Questions related to safety, capacity to infect the vaccinated person and his contacts, potency and indications for use are not yet clarified. Horstmann, Niederman and Paul of Yale University School of Medicine attempt to answer some of these questions (*J. A. M. A.*, 170: 1, 1959). The study conformed to WHO recommendations, and Sabin's LSc type 1 attenuated poliovirus was used to carry out three trials in a closed institutional community. In the course of these trials there was also a limited opportunity to watch an epidemic of inapparent infections under controlled conditions. Attenuated type 1 poliovirus was administered by mouth to selected children in housing units, each of which contained 34 or 35 individuals, up to 20 of whom were fed the virus in any one of the three trials. All of the persons in the unit were at least theoretically immune to paralytic poliomyelitis before the first trial, having either naturally acquired type 1 antibodies or having been vaccinated with Salk vaccine at least twice in the foregoing six months.

Commenting on the results of these trials, Horstmann and his colleagues emphasize that they demonstrate first of all that attenuated poliovirus infections can spread readily in a closed population where contact is intimate and

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MEDICAL NEWS *in brief*

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there are enough susceptible persons present. Local resistance or local immunity was suggested by the finding that reinfection can occur in the presence of significant neutralizing antibody levels, but the naturally acquired antibody resists intestinal infection to a greater degree than that acquired by vaccination with Salk vaccine. Local immunity was obviously absent in a few cases of throat infection which occurred in children previously vaccinated with Salk vaccine when the virus was fed in liquid form rather than in capsules. This did not take place in any of the children with natural immunity who received liquid vaccine. Evidence was obtained that adequate neutralizing antibody levels express something which limits the spread of poliovirus within the body and prevents significant invasion of the central nervous system. Slight increase in virulence of the LSc strain was encountered after the virus had produced human alimentary infection in that the virus isolated from the fæces showed a minimal increase in neurotropism for monkeys.

Plotkin *et al.* of Philadelphia studied the duration of immunity produced by oral administration of living attenuated poliovirus (*J. A. M. A.*, 170: 8, 1959). Three groups of children were available for study. Group A were the first human subjects to be given attenuated virus in 1950-1951, and their serum was found to contain significant antibody titres three, four, five and six years after vaccination. Group B had received the vaccine in 1954 and 1955, and persistence of antibody was demonstrated up to 2½ years after vaccination. In Group C, which included normal infants less than six months old who were fed poliovirus in 1955-1957, serological response was obtained in spite of the presence of natural antibody. The results in general showed that sero-immunity after live-virus vaccination is of long duration. Although there is a possibility that booster infection occurring in nature may contribute to the maintenance of sero-immunity in some of the children, there is good evidence that antibodies persist for many years even in the absence of reinfection. The workers express optimism concerning the usefulness of living attenuated viruses as immunizing agents against poliomyelitis, especially as they demonstrated that vaccination can be successfully performed in early infancy.

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OXYGEN TREATMENT OF WORM INFESTATIONS

A Bulgarian author, Todorov (*Abstracts of Bulgarian Scientific Literature*, 3: 102, 1958), reports his results in a series of 151 cases of infestation with intestinal worms, using the method of Kravetz, which depends on the fact that oxygen inhibits development of some helminths. Through a duodenal tube oxygen is introduced into the stomach [sic] on two successive days to a volume of 1250 c.c. Contraindications include organic lesions of the stomach and advanced pregnancy.

The author states that the results of the treatment were very good in infestation with *Ascaris lumbricoides*, with a cure rate of 85%; infestation with *Trichiuris trichocephalis* and *Hymenolepis nana* was not affected by this treatment.